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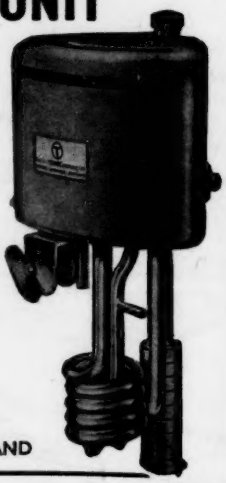

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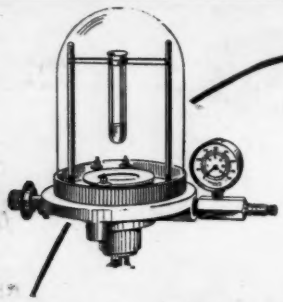

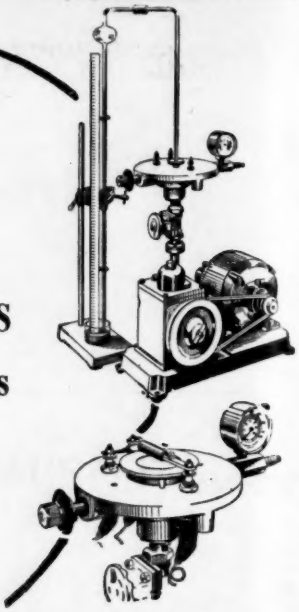

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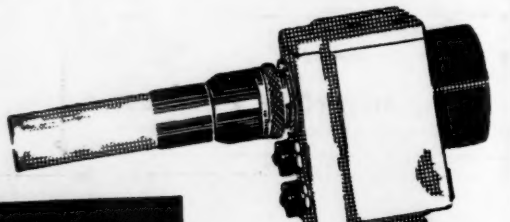

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NATURE

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RESEARCH AND DEVELOPMENT IN BRITAIN

ALTHOUGH the financial provision for research and development in 1955–56 set forth in the Statement on Defence 1955 is about the same as 1954–55, the very magnitude of that expenditure—some £837 million gross—quite apart from the demands that the programme makes on the scientific and technical man-power of Britain, at the least prompts the question whether this effort is in balance with other equally essential demands on the nation's resources of man-power and materials, as well as of finance. The demands of defence must be considered along with those of the programme for nuclear power and of the proposals for the modernization of railways and roads which have also recently been laid before Parliament. Even where no secrecy considerations enter, it is not easy to obtain a clear picture: defence research and civil research are closely interlocked in many fields in addition to that of nuclear energy, and the task of striking a sound balance is far from easy, no matter how closely the Advisory Council for Scientific Policy and the Defence Research Policy Committee are co-operating.

The nation's scientific and technical resources will undoubtedly be stretched to the limit to meet the demands made upon them by the proposals laid before Parliament this session; there will certainly be no room for overlapping of effort or waste of resources. It will be imperative to see that the structure of the nation's research organization is efficient and effective, that it is competent to secure prompt action to redress any weakness that threatens at short term or long range to endanger the national effort. The shortage of science teachers and the position of technical education might be cited as two examples, particularly as they illustrate how any adequate survey must take account not simply of economic resources, industrial and academic research, but also of the conditions which determine the appropriate flow of recruits, at all levels where they are required, to industry and to the university departments, as well as to government departments and the Services. Nor can there be any room for organizations or institutions that are no longer giving full value to the nation, or that are fulfilling functions which would now be more effectively served in other ways.

It has been apparent from the number of Parliamentary questions in recent months that the House of Commons has been particularly vigilant in respect of the Department of Scientific and Industrial Research, while the debates last year on the Development of Inventions Bill clarified considerably the functions of the National Research Development Corporation. Parliament was satisfied in these debates that adequate arrangements were made to prevent overlapping in the development of inventions between the research associations and government departments, and that the extension of the Corporation's borrowing powers for a further five years would not lead to competition between the Corporation and industry or other government departments, but enable the Corporation to promote research and development where it was needed, and was otherwise unlikely to be undertaken. The Corporation's functions were also explained in a number of addresses last year, notably by the Earl of Halsbury to the Royal Society of Arts.

Nevertheless, the Corporation has done well to devote the major part of its fifth annual report* to a general stocktaking of the Corporation's functions and its position in the national economy in the light of its first five years work (see also *Nature*, March 26, p. 541). The review leaves little doubt as to the value of the Corporation, even if its real functions are more limited than was originally supposed, or at the time when Sir Henry Tizard gave his Messel Memorial Lecture in 1952. When the Corporation was formed, it was thought that a single organization for dealing with the exploitation of discoveries or inventions made in government departments or in semi-official research organizations would offer real advantages. It was also believed that the existence of a public body which could assume the responsibility for effecting liaison between centres of learning and research on one hand, and industry on the other, would meet a real need and enable science to be applied to industry and agriculture at an accelerated rate. Thirdly, it was believed in some quarters that full exploitation of the inventive talent of Britain was in part frustrated by lack of support for inventors, particularly amateur inventors without industrial connexions.

It is this third expectation that appears to have been falsified. The Corporation's five years experience has not shown that a multiplicity of meritorious private inventors stand in need of public assistance. One or two good inventions from private sources receive its support each year, and the Corporation may be right in regarding as justified the work involved in assessing the merits of such inventions and the money expended on their development. Outside the field of light engineering and instrument manufacture, it concludes, the isolated individual rarely appears to have any serious contribution to make to the advancement of technology.

The absence of meritorious proposals in the various fields of physics, chemistry, biology, medicine and the non-mechanical branches of the engineering sciences could equally, however, be due to industry being quicker to recognize promising ideas and to outside financial assistance for the private inventor being more easily available than was supposed after the War. Certainly the Corporation's reports afford no support for fears that industry is relying on government bodies for development in matters where the initiative should lie with industry itself. Too much may have been expected of the Corporation in some directions, and equally some of the fears entertained have proved groundless. The Corporation has

* National Research Development Corporation. Report and Statement of Accounts for the year 1st July, 1953, to 30th June, 1954. Pp. 20. (London: H.M. Stationery Office, 1955.) 9d. net.

experienced no difficulty in obtaining first-class opinion on the technical merits of any proposal coming before it, and where such opinions have been favourable, it has accepted its obligation to act upon them. Moreover, in agreement with its advisers, it has made small beginnings in untried fields and has in consequence spent much less than was originally provided to finance its activities.

The demonstrable field for the Corporation's activities lies in the development of government inventions and those made by other public research bodies. The Corporation believes that the needs of this group have largely been met. The Corporation is now administering on commercial lines some thousands of British and foreign patents and patent applications, and these patent rights are beginning to earn revenue which should rise slowly but steadily with the years.

A major difficulty encountered by the Corporation has been to decide whether a proposal before it should be viewed as research having for its object the making of a new invention, or as research having for its object the development of an invention already made. Such difficulties tended to arise wherever joint enterprises between the Corporation and the public research establishments were contemplated. The wider powers given in this respect by the Development of Inventions Act, 1954, have removed this uncertainty, and while it is unlikely that many new projects will be called into existence, it will be easier in future for the Corporation to decide whether a given project falls inside or outside its statutory functions.

The Corporation has also encountered a major difficulty through the injunction to entrust the exploitation of inventions "to persons engaged in the industry concerned", an injunction which does not extend to development. The Corporation may, for example, place a development contract with a firm not in the industry; but a licence for manufacture, special circumstances apart, may only be given within the industry. A development contract thus placed tends on one hand to bring a contract into the industry and to create a "special circumstance" in the special knowledge and skill acquired by the contractor. Moreover, the more novel an invention is, the less obvious it is which of various industries can fairly claim to be the industry most concerned. The Corporation has taken the view that it is required to avoid introducing unfairly competitive elements into a recognized industrial pattern; but not, where no clearly defined pattern exists, to avoid all initiative for fear of changes which profound novelty must introduce.

The Corporation is not a trading concern, although since an isolated development contract unrelated to sufficient initial orders to test the market has proved an inadequate means of securing its aims, the Corporation has sometimes found it essential, with the approval of the Board of Trade, to give contractors sufficient initial orders to enable them to undertake production. This has been done notably with the electronic digital computors, for which the Corporation has underwritten both development and initial stages of production. Apart, however, from any profits derived from the Corporation's initial interest in commercial manufacture and sales thus underwritten, its only assets are the patent rights in the inventions which it runs, and under which it grants licences in consideration of royalty payments. These are wasting assets with a useful life of sixteen years, and it is probable that a further five years will be required before the Corporation's financial prospects can be reasonably assessed.

Despite this caution, the Corporation is convinced that its work serves a useful purpose at a relatively modest cost. The report points out that industry is less homogeneous and continuous than is frequently supposed. This probably provides the Corporation with its greatest opportunity, next to the exploitation of government inventions, by establishing communications between two parties to a discovery which affects them both, as happened when the Medical Research Council discovered that waste sisal juice was a relatively copious source of hecogenin, a possible starting point for the synthesis of steroid hormones such as cortisone. There were no pre-existing lines of communication between the sisal plantations of the tropics and the pharmaceutical industry of Great Britain, and no means by which the former could ascertain whether the latter would, in fact, wish to use hecogenin, while the latter had no hecogenin for experiment and thereby to establish a price which it could offer. The Corporation commissioned a pilot plant in Kenya, underwrote a full-scale plant to be erected on a sisal plantation in Tanganyika, contracted for the output and placed a development contract for the refining process before firms in the pharmaceutical industry had given any clear indication that hecogenin would be wanted.

That within two and a half years of the Medical Research Council's discovery a British firm has been enabled to begin small-scale production of cortisone in the United Kingdom based on hecogenin produced in East Africa and the West Indies may well seem sufficient justification for the existence of the Corporation. The argument that there is a special service to be rendered to the community in this context is not invalidated by the fact that the original expectations in regard to cortisone have been disappointing. The urgency was there, and the clinical value could not be established until sufficient supplies were available for trials on an adequate scale.

This example sufficiently indicates the importance of the work of the National Research Development Corporation becoming widely known. The survey of the relations between industry and science in the Greater Manchester area made by the Manchester Joint Research Council left the impression that the Corporation was not yet sufficiently widely known to play effectively the part it was created to fulfil. The Corporation's expenditure, even its consolidated balance sheet, looks trifling compared with the national expenditure of approaching £200 million on civil research and development and of £837 million on defence production and research; but it is none the less essential that full use should be made of the Corporation's services wherever appropriate.

That is, of course, one particular aspect of the broad problem of securing the widest dissemination of knowledge and the effective utilization of research results by industry. It may be recalled that the last annual report from the Advisory Council for Scientific and Industrial Research referred particularly to the relations of the Corporation with the research associations. Some research associations are already using the Corporation as the normal agent for the development of inventions. Others, such as the cotton industry, the coal utilization and the electrical and allied industries research associations have adopted the policy of forming analogous companies to take over their inventions and discoveries for development on a business basis. Such a system has the advantage of relieving a director of research and his staff of responsibilities which may be outside their normal training and experience, and transferring them to a board of directors and management experienced in the financial and economic problems involved in development. It presupposes, however, that a board and management of the requisite experience and sound judgment can be found, and it also ignores the possibility that development problems, while onerous, may not be without value in widening the outlook and experience of a director of research and his staff and consolidating his judgment in the selection of problems for research.

The real lesson to be drawn from this quinquennial review of the work of the National Research Development Corporation's work, and the reason for discussing it at length, are the demonstration the review affords of the value of a critical and constructive review of all aspects of the nation's research effort at a time when it is being kept at full stretch. Only by such means can we be sure of eliminating inefficiency or waste, and of making the necessary adjustments when one function becomes obsolete or is better served by other means. That is particularly true when the functions of an organization appear to be changing, as, for example, with the research organizations, the educational functions of which have since the War come to assume much greater importance, both from the point of view of introducing new ideas and new knowledge to industry and of training technical and scientific staff.

For this reason alone it is reassuring to learn that special surveys of the resources, programmes and facilities of the research associations are proceeding, though it would clearly be unreasonable to expect effort to be expended on more than one or two such surveys at any one time. Nevertheless, there is some reason for believing that direction at a higher level is not so clear or so far-sighted as is desirable. This could be sensed in the last annual report of the Department of Scientific and Industrial Research, and in the meagreness with which the office of the Lord President of the Council is staffed, as well as in the continued absence of a direct spokesman for the Lord President in the House of Commons.

It is still more apparent from the reply given by Mr. J. R. Bevins, Parliamentary Secretary to the Ministry of Works, on behalf of the Lord President, when questioned about the cutting down of operational research by the Building Research Station. The Government believes that productivity in the building industry has increased by about ten per cent in the past four or five years, and that operational research in the industry is now not so necessary. This reply will leave the ordinary citizen unconvinced. There is no need to look far for evidence that, whatever the general increase in productivity since 1950–51, it has not been general throughout the industry, and it does not balance the loss of efficiency since 1939. The industry compares badly in this respect with some other industries, and is notoriously backward in adopting the new techniques, materials and practices which the work of the Building Research Station and other advances in scientific knowledge have put at its disposal.

We are thus concerned with something more than the climate of opinion to which Lord Salisbury referred in the speech read in his absence by Mr. Selwyn Lloyd at the annual luncheon of the Parliamentary and Scientific Committee. That Committee could well help, as Lord Salisbury suggested, to create an outlook more favourable to the utilization of science in industry, and the wider employment of scientists and technologists in managerial positions. It could also help with the task of securing a wider dissemination of the knowledge of technical developments and the results of scientific research, as well as in securing a continuous and practical approach to the problem of overcoming the human obstacles to innovation at all levels. But the Committee's first task, and one which no other body could so effectively discharge, may well be to see that the Government keeps constantly in mind the necessity of seeing, not merely that adequate resources are available for scientific and industrial research and development, but also that the organization by which these resources are administered and co-ordinated is appropriate and adequate to its purpose, used with energy and vision and intelligence and continuously reviewed in the light of changing national needs. It should at least see that the right questions are asked about the distribution of Britain's research effort, about its organization and financing as from public and private sources and about the recruitment of trained man-power and the supplies of equipment and material. More than most other bodies, it has the status to ensure that reasonable answers to such questions are forthcoming from the Government.

BIRD DISPLAY

Bower-Birds

Their Displays and Breeding Cycles—a Preliminary Statement. By Dr. A. J. Marshall. Pp. x+208+27 plates. (Oxford: Clarendon Press; London: Oxford University Press, 1954.) 30s. net.

DR. MARSHALL has been studying the biology of the bower-birds, both in the field and the laboratory, for the past twenty years, and has published a number of papers upon the subject from time to time during that period. In this volume he collects together the accumulated results of his own researches,

together with everything that is known from other sources about the lives of the bower-birds. The result is an admirable book which the author modestly calls "a preliminary statement" and a "basis for further research", and which forms a valuable contribution to scientific ornithology.

The bower-birds, which with the cat-birds form the family Ptilonorhynchidae, are passerine birds of moderate size confined to Australia and New Guinea; they have long been known to build display grounds and to decorate them with various brightly coloured or otherwise conspicuous objects. The bower is built on the ground and has no direct connexion with the nest, which is made in a tree, often at a considerable distance. Some species even paint their bowers with fruit-pulp, wet charcoal, or comminuted dry grass mixed with saliva, and one species makes a 'paint brush' to help it apply the decoration. The bower of another species, decorated with living orchids, may reach a height of nine feet; and a gardener bower-bird of New Guinea builds a hut and plants a meadow of moss before it which is decorated with coloured fruits, flowers and fungi. On the display ground of the spotted bower-bird of Australia, coins, jewellery, car keys and other decorations stolen from human habitations are sometimes found. Most of the species are strikingly skilful vocal mimics of other birds, and their noisy and spectacular displays often take place outside the breeding season.

In the literature that has grown up about the activities of the bower-birds, it has become accepted that the motive for making and using bowers is a consciously æsthetic one, that sexual motivation has little or no part in bower-building and the associated phenomena, and that the birds 'play' at playgrounds rather than display. The author shows that such ideas are no more than anthropomorphic nonsense, and that apart from purely descriptive matter little that has been written about the behaviour of the birds can withstand critical inquiry. As a result of his histophysiological studies, Dr. Marshall shows that "these complex and remarkable phenomena are probably expressions of innate behaviour patterns that are annually brought into play by the secretion of sex hormones during the period of pre-nuptial testis modification, which begins at approximately the same time each year, except in birds that inhabit dry areas of spasmodic and uncertain rainfall. . . . The display, which may continue for months, attracts and retains the female's interest, keeps off rivals, and helps synchronise the male and female reproductive processes until, when the environment becomes seasonally appropriate for nesting and the rearing of young, fertilization occurs and the female goes off to build her nest and to rear her young without masculine assistance".

In his chapter on the evolution of bower-building, the author points out that sexual display is universal throughout the class of birds, and that display-grounds are used by many species, as, for example, the black-cock and the ruff. He suggests that the extraordinarily elaborate display grounds of the bower-birds are no more than a special and very interesting case of this widely spread phenomenon, in which the similarities are examples of convergent evolution. Even within the family Ptilonorhynchidae the development of display mechanisms has evolved independently in the bower-birds and the cat-birds, and the similarities are the result of convergence.

The author devotes separate chapters to describing all that is known of each species of the family, but gives more space to the satin bower-bird than the others, for this is the species which has been most available to him for experimental work. His book is of great value in correlating field observation with histophysiological work in the laboratory, and is a splendid example of the best modern trend in the study of natural history. There are numerous excellent illustrations. L. Harrison Matthews

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A STUDY IN PALÆONTOLOGY

Life of the Past

An Introduction to Paleontology. By George Gaylord Simpson. Pp. xii+198. (New Haven, Conn.: Yale University Press; London: Oxford University Press, 1953.) 4 dollars.

ANY work from the pen of Prof. George Gaylord Simpson merits attention, whether it be geographical, statistical or palæontological. He is so much at home in so many fields and in so many languages that one may at times be apt to forget that his descriptive palæontological work is unsurpassed. By that I mean to imply that he sees both the wood and the trees and he never forgets the implications of either.

This present volume is perhaps the least serious of his recent writings. He has lately managed to survey evolution in a way that would have given most authors the right to a pause in their labours, so presumably this might be expected to be a classic, though a lesser classic. Instead of this, I venture to suggest that it is one of the most important palæontological works that has appeared for some time, because it contains precisely what the student should bear in mind when he approaches the study of the past forms of life. It may be well and astonishing that one take the shell or a bone of a long-gone animal and tell its name and its age. It could be impressive if one were able to do this with a great number of fossils, and it would yet be possible for such a geological exhibitionist to have very little idea of the circumstances of the past.

To understand the true nature of a specimen, one must realize the age in which it was placed; the geography of the time; its animal and plant competitors; the whole to be seen against the background of its predecessors and successors and on the scale of time.

This is more or less what Simpson does here. Using the ample resources of the United States for most of his examples, he discusses the evidence on the ground and proceeds to explain how the evidence got there. Step by step he describes the reconstruction of the once-living animal from its shell or skeleton, and builds up the communities in which it lived. It is then easy to discuss the evidence that collections of fossils give as to the geological and zoological nature of the past. Knowing how an animal is constructed and the place where it was adapted to live enables one to derive a good idea not only of its complete anatomy but also of its physiology and therefore of its degree of adaptability.

With this kind of information one can speculate not only on the diversity of life but on its essential ability to diversify.

This leads naturally to the discussion of organic change and the theories of evolution; but the whole is done in comparatively direct and simple language

and with a wealth of reference to interesting observations and discoveries that the author has made. For those who demand something more for the examination table, there is a short appendix of the forms of life arranged systematically. There are also a list of books suggested for further reading and a good index. Indeed, the only thing one can complain about are the illustrations, which are unnecessarily sketchy and crude for a book that is otherwise produced on a standard commensurate with its price.

W. E. Swinton

OBITUARIES OF THE PILTDOWN REMAINS

Further Contributions to the Solution of the Piltdown Problem

Bulletin of the British Museum (Natural History): Geology, Vol. 2, No. 6 (1955).

The Piltdown Forgery

By Dr. J. S. Weiner. Pp. xii+214+8 plates. (London: Oxford University Press, 1955.) 12*s.* 6*d.* net.

THE Piltdown saga has now been concluded. The British Museum (Natural History) has brought together under the title "Further Contributions to the Solution of the Piltdown Problem" in its Bulletin (Vol. 2, No. 6) the views of a large number of specialists who have described their work on the specimens—work which has resulted in demonstrating without any doubt that the whole thing was a hoax. This is an important publication, as we have here, clearly set out, the methods now at our disposal to check discoveries, and are shown how they demonstrate that the Piltdown finds were not genuine. These methods have to some extent been perfected as a result of the Piltdown re-investigation, and to that extent the 'hoax' has been useful. The late Sir Arthur Smith Woodward had not these methods of study at his disposal and therefore cannot be blamed for having failed to spot the imposition. Unfortunately, he had casts made almost at once, which were mainly used by savants when studying the specimens. No cast, however well made, can give the minute scratches such as those which in the case of the teeth were of great significance. I was a youngster at the time and never a 'bone' man; but I was one of a not too numerous band who was allowed to handle the originals in Smith Woodward's room at the Museum soon after they had been presented at a meeting of the Geological Society. But even if I had had the knowledge to judge the matter, it would not have occurred to me to question their authenticity.

Dr. J. S. Weiner's book, "The Piltdown Forgery", deals rather with the many personalities in the case. For this reason it will have a very popular appeal. It is exceedingly well written and gives one a vivid picture of the group of keen amateurs, most of them friends of old Ben Harrison, of Eolithic fame, who were concerned at the time with Sussex geology and archæology. We are led relentlessly to one conclusion, which, though it can never be absolutely proved, is the only one which fits the facts. The story unfolds with the discovery of Piltdown I, and we find not a few of the local amateurs a little suspicious that all is not as presented. We now have evidence for staining of specimens; we have the 'happy' find of Piltdown II which was to clinch the matter. There was even more in the background which never appeared until much later.

It all reads like a novel, and I have no intention of spoiling it for others by saying more. It is a book to be read with interest and profit. Such a hoax nowadays is impossible; but it was one actually perpetrated and it was a great success.

Miles C. Burkitt

TREATISE ON VITAMINS

The Vitamins

Chemistry, Physiology, Pathology. Edited by W. H. Sebrell, Jr., and Professor Robert S. Harris. Vol. 1. Pp. xiii+676. Vol. 2. Pp. xiii+766. Vol. 3. Pp. xiii+665. (New York: Academic Press, Inc.; London: Academic Books, Ltd., 1954.) Vols. 1 and 2, 16.50 dollars each. Vol. 3, 15 dollars.

DURING the second half of 1954 these three volumes have appeared in quick succession, and the series is now complete. It is a monumental undertaking, and will immediately take its place as a standard reference work, and source book, for everyone doing research on the biochemistry of vitamins. The scope of the enterprise is apparent from the fact that Vol. 1, running to 676 pages, has four chapters dealing with vitamin A, vitamin C, vitamin B_{12}, and biotin; Vol. 2, in 766 pages, covers six further vitamins (choline, D, "F", inositol, K, nicotinamide and pantothenic acid), while Vol. 3 in 665 pages takes up the topics of PABA, folic acid, B_6, riboflavin, B_1, E and other factors.

Each chapter in turn contains a dozen or so sections, by separate authors, dealing successively and systematically with such matters as nomenclature, chemistry, industrial preparation, biochemical systems, specificity of action, biogenesis, assay, standardization, distribution in foodstuffs, effects of deficiency in animals, deficiency in human beings, pharmacology, pathology, requirements of animals, and human beings, and even "future problems". The individual sections are further split up into sub-sections, and these into sub-sub-sections. There is no doubt that this is far and away the most comprehensive treatment of the subject that has so far appeared in a single treatise. Nevertheless, it is not exhaustive. The clinical manifestations of vitamin deficiency and their treatment are not described in any detail, nor are the methods of vitamin assay, the reason given being that these matters are already fully dealt with elsewhere.

The undertaking is essentially American. (In Vol. 1, seven of the eleven authors are from the United States, two from Germany, and two from Britain. In Vol. 2, of the nineteen authors, seventeen are American, and the remaining two Canadian. In Vol. 3, twenty-two authors are American, and one is Dutch.) It is in consequence of this fact, perhaps, that in several of the sections the bibliography does not quite fairly cover the whole of the international scene, but deals too exclusively with the American literature, which is presumably more accessible but, chronologically speaking, not always the 'first in the field'. All the same, any serious investigator desiring to make contact with the existing scientific literature could not do better than start the search with "Sebrell and Harris". We owe a debt of gratitude to the editors and to the authors for their most successful endeavour.

Leslie J. Harris

EMIL BEHRING AND PAUL EHRLICH

THEIR CONTRIBUTIONS TO SCIENCE

By Prof. C. H. BROWNING, F.R.S.
Emeritus Professor of Bacteriology, University of Glasgow

MARCH 14 and 15, 1954, marked the hundredth anniversaries of the birth of Paul Ehrlich and Emil Behring—two men whose achievements have had a profound effect on the trend of biological science and medical practice in the past fifty years. Biographical accounts of them and bibliographies are readily accessible; it need only be noted that both came from the German middle-class and apparently neither stock had any close medical connexions. Here an attempt is made to place their chief contributions in the perspective of their own time as well as the present day.

EMIL BEHRING[1]

Behring made the great discovery of the class of biological products known as antibodies. In 1890 he published along with Kitasato evidence that the soluble poison (toxin) of the tetanus bacillus, when injected into the tissues of living susceptible animals under conditions appropriate for developing immunity, leads to the appearance in their blood serum of the property of neutralizing the toxin. This was attributed to the development of 'antitoxin', the first example of an antibody which is produced in response to the stimulus of an antigen, here the toxin. Diphtheria toxin behaves similarly. Shortly before this, Roux and Yersin had proved that the pathogenic effects of diphtheria bacilli are completely reproduced in susceptible animals by injecting their toxin; and the same is true of tetanus. (The term 'toxin' or 'exotoxin' was applied to crude fluid cultures of the organisms rendered sterile by passage through fine-pored filters; but recently progress has been made in obtaining chemically pure toxins, which are of protein nature.) A quantity of toxin which is a large multiple of the fatal dose can be rendered innocuous by the previous addition *in vitro* of an appropriate amount of antitoxin. Further, antitoxic serum when injected into a normal individual renders the latter immune, such immunity being termed *passive* in contrast to the *active* immunity of the animal which has received the toxin. Thus, clearly an animal which has been treated by injections of toxin is immune to the disease in virtue of developing the antitoxin. Antitoxin has curative, as well as protective, action, because after injecting a dose of toxin which otherwise would be fatal, it is possible to save life by afterwards administering antitoxin, although the length of the permissible interval is limited. The phenomena were recognized as being specific, since diphtheria antitoxin does not confer immunity against tetanus or vice versa.

The practical implications of Behring's work for medicine were rapidly grasped. At that time diphtheria was a very prevalent and highly fatal disease in Europe and America. Treatment with antitoxin was soon established, and although there may be few recorded series of trials which would satisfy strict statistical criteria, the opinion among physicians of its high therapeutic value quickly became practically universal. The efficacy of tetanus antitoxin in preventing tetanus in man was confirmed on an impressive scale in the First World War. In 1901 Behring received a Nobel Prize for his pioneer work on serum therapy, especially against diphtheria; he was also created von Behring. Apparently his earliest research, on iodoform, then regarded as a valuable drug in the local treatment of pyogenic infections, but now fallen into disuse, suggested that for effective therapy of an infection it was not essential that the causal organism should be killed by the medicament, and in antitoxins he saw the evolution of this principle. It must be noted, however, that relatively few species of pathogenic bacteria act in virtue of producing powerful exotoxins, and therefore only a limited number of infections are capable of being effectively countered by antitoxins.

Behring's later investigations were largely concerned with tuberculosis, especially active immunization by vaccines which he prepared; they did not yield valuable results. He recommended a mixture of diphtheria toxin and antitoxin for active immunization of the human subject against diphtheria, which proved effective. Owing to risks in use, it has been superseded by safer preparations containing toxoid, especially toxin treated with formaldehyde, which destroys its toxicity without damaging the antigenic properties. As will be seen later, treatment by diphtheria antitoxin became a practical success largely through Ehrlich's work on standardizing its potency; his method of test ensured that the products were, in fact, effective.

The discovery of antitoxin and its spectacular action in diphtheria greatly stimulated inquiry into immunity mechanisms. Various other manifestations of antibody action were disclosed and antibody formation was found generally to accompany acquisition of immunity to pathogenic organisms or their products. The demonstration that antibodies may be necessary in order to render certain virulent organisms susceptible to phagocytosis reconciled the humoral theory of immunity with Metchnikoff's cellular doctrines. The fact that antibodies can be developed to a number of foreign substances which are innocuous, for example red blood corpuscles of other species, proved that they are a product of biological reaction of the tissues which has no necessary connexion with disease. It is of great interest also that natural antibodies occur, for which no known antigenic stimulus can be traced. Antigens usually contain protein, and it is the rule that to be effective they must escape degradation in the alimentary tract, hence generally they must be introduced parenterally. The investigation of antigens and antibodies has developed into an active department of science in its own right, serology, which has yielded many important applications in addition to therapy, for example in diagnosis of the species of animal products, identification of micro-organisms and the recognition of infections which they cause, as well as elucidation of the morbid manifestations

associated with allergy and hæmolytic diseases. The remarkable specificity of antigen–antibody reactions in a physical–chemical sense dominates this field of inquiry.

PAUL EHRLICH[2]

Ehrlich was an incessant worker: from 1877 on he made outstanding original contributions, and although the last publications under his own name appeared in 1913, there is no sign that his intellectual faculties were failing. However, he used to complain of the sterilizing effect of controversy, when the objections of others compelled him to devote attention to matters which he considered to be settled. In 1914, to commemorate his sixtieth birthday, there appeared under the title "Paul Ehrlich" an account of his scientific work. The sections of this *Festschrift* which treat of special topics are by thirty-one authors, and there are more than six hundred titles of papers in the names of Ehrlich, members of the staff or visitors in his laboratories. As he died in the following year, this is almost a complete record.

Waldeyer, the anatomist, told how he once came on Ehrlich when a medical student in his second semester and a beginner in histology, staining preparations with various dyes which Ehrlich himself had selected for trial. This incident gives the keynote to his life-work—chemistry devoted to furthering biological knowledge. The chemistry was from choice that of the organic dyes, a branch rapidly developing in Germany at the time in industrial as well as academic laboratories. The biology, while it ranged widely, comprehended especially mammalian physiology and pathology. Ehrlich was no man's disciple; he was mainly self-taught, and largely created his own fields of research. At first the laboratory work was done by his own hands; but by the beginning of this century the control of a large institute at Frankfurt-am-Main, as well as the financial support of friends, afforded ample official and unofficial assistance. Even then, however, he did not desire the numbers which are now not uncommon; he wished no more than he could completely share working experiences with, and avoided "many doves flying in and out". His formulations of theory, although often hammered on the anvil of his assistants' brains, were his own creations.

Ehrlich's subjects of investigation may be arranged more or less in chronological periods, but the earlier studies, such as those on staining of the blood cells, made the least demands on material resources. Then came the investigations on toxin and antitoxin, which culminated in an accurate method of standardizing diphtheria antitoxin. Out of this arose also the statutory control of antisera and other biological products used in medicine, which was a main function of the Königliches Institut für experimentelle Therapie. This led to other investigations on immunity mechanisms made possible largely by the tools which Bordet's discovery of hæmolytic immune sera provided. In addition, Ehrlich devised the side-chain theory to account for the action of toxins on the basis of his conception of normal processes of nutrition and to explain the development of antitoxins and other antibodies. The theory aroused the widest attention and met with immediate and almost universal acclaim. Ehrlich's reputation had now gained the standing which made it possible to undertake his cherished plans for chemotherapy. This was the most expensive of his researches in the demands on materials and skilled assistance in chemistry and various departments of pure and applied biology. Investigations on cancer were carried out largely in response to the wishes of public and private supporters and proceeded concurrently with studies on immunity and chemotherapy. Chemical research went on throughout, and was in later times his only handiwork.

Ehrlich, like Faraday, was above all a born experimenter. His principle of work is illuminated in a quotation from his notes translated in Miss Marquardt's book as follows: "During my work as a student I repeatedly tried to follow up certain lines of thought by experiment. But I did not succeed in carrying out a single one of my ideas in this way. Soon, however, I came to try the other way round, that is to say, not to give directions to Nature but simply try to analyse striking experimental facts which were difficult to understand and by so analysing to find the laws which governed the action". The initial stages would appear 'empirical' to some, but so is all exploration unless informed by the best scientific practice of the time, as Ehrlich's emphatically was. His deep knowledge of both chemistry and biology enabled him to recognize associations hidden from others.

Tinctorial Analysis

Until late in the 1880's Ehrlich's research consisted chiefly of *Farbenanalytische Studien*. His first discovery was that the connective tissue contains cells packed with large granules which have an affinity for basic organic dyes; the granules are also metachromatic, acquiring a tint different from that of the cell nuclei or the dye in aqueous solution. Dahlia, dissolved in a suitable mixture of water, alcohol and acetic acid, stains only these granules. Thus for the first time—excepting madder and bone—a selective histochemical reaction for a normal tissue constituent was got; this contrasted with previous morphological staining by carmine, etc. The cells were called mast cells (from the German for 'feeding up' of animals), because they are specially numerous in 'overnourished', that is, stimulated, connective tissue. Ehrlich subjected the leucocytes to similar examination, using dried blood films one cell thick and fixing them by heat, as in Koch's procedure for bacterial cultures. The films were stained with 'triacid' and other dye mixtures which Ehrlich devised. He distinguished, in addition to basophils, specific lines of eosinophil (acidophil) and neutrophil granular leucocytes, as well as non-granular forms. This laid the foundation of morphological hæmatology and permitted an exact classification of the leucocytoses—and hence correct inferences as to underlying causes—and the differential diagnosis of leukæmias. The composition and exact functions of the various granules have not yet been fully elucidated. Mast cells contain stores of heparin and histamine, also perhaps hyaluronic acid[3]; the eosinophils and neutrophils are rich in oxidase and the latter contain proteolytic enzymes; but beyond that little is known. Studies of the nucleated and non-nucleated red blood corpuscles enabled megaloblastic and aplastic anæmias to be separated from the commoner normoblastic type associated with what is now called hypochromic anæmia. The examination of the red bone marrow, so valuable an adjunct to blood examination, is a direct development of Ehrlich's original work. Another important discovery of this period was the application of

methylene blue as a highly selective stain for micro-organisms, with little affinity for tissue elements except nuclei and mast-cell granules. Also, the acid-fast property of the tubercle bacillus was demonstrated; without it the microscopic examination of pathological materials for this organism would have remained an academic accomplishment, instead of becoming one of the simplest, as well as most reliable, diagnostic procedures.

Vital staining, which we owe to Ehrlich, constitutes a fundamental advance in the methods of studying the tissues of the living animal. He recognized the great biological significance of being able, as it were, to mark constituents of normal cells in full functional activity and not merely inspect them *post mortem*. Certain dyes in solution are taken up in characteristic fashion without producing any obvious harmful effects. Thus methylene blue (and some other thiazine dyes) on injection into the circulation colours ganglion cells, nerve fibres and endings—why some of them remain unstained is not clear, although Ehrlich suggested that a lowered alkalinity and oxygen-saturation were factors. Vital staining with methylene blue provided a new means for investigating the microscopic anatomy of the central nervous system and yielded valuable results. Neutral red, also a basic dye and very little toxic, stains granules, so far of undefined constitution, in various tissue cells, but nuclei are coloured only after cell-death. Some acid dyes, such as isamin blue, trypan red and trypan blue, are taken up especially by the histiocytes, and conspicuous stained droplets appear in the cytoplasm. As these cells have the property of ingesting micro-organisms and other solid particles, it has been surmised by later workers that the 'segregation apparatus' acts as an immunity mechanism and may have an important association with antibody production.

In "Das Sauerstoff-Bedürfniss des Organismus" (1885), Ehrlich tackled the problem of comparing the oxygen requirements of tissues in the living animal. The work, which was tentative and speculative, broke new ground by means of a novel experimental method, namely, the introduction into the tissues of dyes capable of reversible reduction and oxidation; but differing in the ease with which reduction from the coloured to the leuko form can be effected. In order to obtain satisfactory results it was found necessary to use compounds of very low solubility in water, which, however, yield colloidal solutions, and the degree of dispersion is an important factor for the staining. The dyes were alizarin blue, which is reduced to the colourless form with difficulty, and indophenol blue, which is easily decolorized; the energy required is, of course, capable of measurement. Both compounds circulate in the blood in the coloured state. After administration of the substances (in toxic doses) to rabbits, etc., the animals were examined at an appropriate time. The organs were inspected on removal immediately *post mortem* to avoid changes in the dyes occurring later, and they were parboiled or squashed between glass plates to reduce the masking effect of their natural colour. The following findings relate to circumstances where flooding of the circulation with dye has been obviated and the respective organs have a considerable affinity for it. The heart, cerebral grey matter and striped musculature do not reduce alizarin blue and so are stained (although reduction of the dye occurs soon when the organs are kept in the air). The same is true of indophenol blue, except that it is reduced by certain striped muscles. Accordingly, those tissues are in a high state of oxygen saturation during the life of the animal. On the other hand, the lung, kidney-cortex and liver, as well as, in the cat, adipose tissue, reduce alizarin blue; consequently, these are much less saturated with oxygen. It should be noted that no tissue which reduced alizarin blue *in vivo* failed to reduce indophenol blue. Ehrlich's conclusions that there exist in the body sites with such different affinities was opposed to the view of Pflüger that all tissues are in a state of saturation with oxygen. The above is a bare summary of some of the more clear-cut experimental data and their discussion. The following quotation from the section headed, "Considerations on the fundamental properties of protoplasm" is important, since it states the essence of the side-chain theory: "we may accept that in living protoplasm there is a central grouping of special structure which determines the peculiar and specific activity of the cell, and also that atoms and atom-complexes are attached to this grouping as side-chains, which are of subordinate importance so far as the specific function of the cell is concerned, but not for its collective life".

Immunity

Investigations on immunity (1893 – *c.* 1903) comprised work on toxins, their constitution and mode of action, the development and structure of antitoxins, the standardizing of diphtheria antitoxin and the side-chain theory, followed by studies on cytolytic antisera, especially hæmolysins.

After Behring and Kitasato's discovery of antitoxins the question remained undecided whether the neutralization of toxin by antitoxin is a direct reaction between the two or, since the test object is a living animal, it may depend on some essential biological factor operated by the latter. Ehrlich found that the poisonous plant proteins, ricin, abrin, etc., develop antitoxins in animals; and the hæmagglutinating property of ricin for a saline suspension of red blood cells *in vitro* is abolished when antiricin serum has been added to the ricin beforehand. A mixture which is neutral as assessed in this way is also devoid of toxicity for test animals. This was the first instance of the use of test-tube experiments in the investigation of a problem in immunity. These facts provided strong evidence that antitoxin acts directly on toxin, the proof being completed by Martin and Cherry.

As already mentioned, the clinical use of diphtheria antitoxin was hampered at first by lack of a method for ensuring that potent sera were available. Ehrlich applied his experience of antiserum production to securing a proper plan of dosage of toxin in the animals to be immunized; also, the use of horses was adopted, as at the Institut Pasteur. He then devised a method of standardizing antitoxin which has remained in practically universal use to the present day. Many specimens of diphtheria toxin were prepared and tested in animals. Guinea pigs of medium weight (250 gm.) were found to be very uniformly susceptible, so that with a specimen of toxin the minimum lethal dose, that is, that causing death acutely, could be accurately estimated. However, the lability of toxin on keeping precluded its use as a permanent standard. Mixtures of a fixed amount of toxin (a considerable multiple of the minimum lethal dose) with varying amounts of antitoxin were tested in parallel and the smallest amount of serum required to neutralize the toxin was ascer-

tained. Supposing that x c.c. of antitoxin were required to neutralize 50 minimum lethal doses, then 10 x c.c. were necessary to neutralize 500. Accordingly, the law of constant proportions holds, and this is true over a wide range of dosage. Different specimens of toxin were tested with a given antitoxin and it was found that the number of minimum lethal doses neutralized by a fixed amount of the serum might vary considerably. Antitoxic serum, when dried and kept *in vacuo* in a cool dark place, retains its potency unchanged for an indefinitely long time; therefore, it is suitable as a standard. The unit is the smallest amount which completely neutralized 100 minimum lethal doses of the toxin originally used, when the mixture in constant volume was injected subcutaneously. But afterwards it proved more practicable to use a mixture containing sufficient excess of toxin to cause death in four to five days, that is, a mixture containing the equivalent of one minimum lethal dose free (animals which survive for this period live for some time, for example weeks or longer). This end-point is more readily determined than complete neutralization as defined by total absence of symptoms and lesions.

The procedure in titrating a new specimen of antitoxin is as follows: (1) ascertain the minimum amount of an available specimen of toxin which is neutralized by one unit of the standard antitoxin to the extent that animals receiving the mixture die on the fourth to fifth day; this is the test dose of toxin; (2) ascertain the maximum volume of the new antitoxin which neutralizes similarly the test dose of toxin; this volume then contains one unit of antitoxin. As was shown later by others, the titrations can be carried out more economically and rapidly by injecting the mixtures in small amount intracutaneously; the amount of toxin used is the least which when injected along with, say, 1/500 unit of antitoxin produces a minimal inflammatory reaction of the skin at the site. Afterwards Ramon demonstrated that when toxin and antitoxin are mixed *in vitro* under suitable conditions, flocculation occurs and, in general, when varying amounts of antitoxin are added to a fixed volume of toxin, that mixture which first shows flocculation corresponds with the neutral point as ascertained by Ehrlich's method. Owing to certain anomalous results, however, the *in vitro* procedure cannot replace animal titration. The flocculation reaction has revealed that one antitoxic serum may cause flocculation more rapidly than another, although the unitage of both may be the same, that is, the 'avidity' of the two differs. Ehrlich's view has been widely accepted that the curative value of an antitoxic serum corresponds with its unitage as measured by his method. Now it is conceivable that differences in avidity might affect the curative action, a less avid serum being the less efficacious, and this has been stated, although substantial evidence on the point is lacking.

Regarding the mechanism of the reaction between toxin and antitoxin, Ehrlich concluded that they behave as substances with strong chemical affinity. Certain experimental findings have to be reconciled with this view, namely: (1) the effect of partial saturation of toxin by antitoxin—if a series of mixtures containing a fixed multiple of the minimum lethal dose of toxin with increasing fractions of the neutralizing dose of antitoxin are tested for toxicity, in general, the smaller amounts of antitoxin neutralize relatively more toxin than the higher amounts; (2) the Ehrlich phenomenon—the difference between the amount of toxin which is just neutralized by one unit of antitoxin and that which when mixed with the same amount of antitoxin proves lethal in 4–5 days, that is, behaves as if it contained one minimum lethal dose of unneutralized toxin, always exceeds one minimum lethal dose and often is much more; (3) the Danysz phenomenon—a fixed amount of antitoxin neutralizes more toxin when the latter is added all at once than when the toxin is added in several portions at intervals. Ehrlich regarded these facts as evidence that crude toxin consists of a mixture of components with differing toxicity and combining affinity; he applied the name toxoid to constituents which are devoid of toxicity, but retain the capacity for combining with antitoxin. Two further points were emphasized by Ehrlich: (4) he stated that the addition of a small initial amount of antitoxin might leave the toxicity unaltered; to explain this he postulated the presence of some toxoid (prototoxoid) with a higher affinity for antitoxin than that of the toxin; (5) the late occurrence of paralysis, etc., in animals which had received 'neutral' mixtures of toxin and antitoxin was attributed to a special poorly neutralizable toxic component of crude toxin, which he called toxone. Prototoxoid has been dismissed by critics as an error of observation—a fault to which Ehrlich was not prone. The effects attributed to toxone appear to have been reproduced by prolonged administration of toxin alone in minute doses. Ehrlich insisted that those who held that crude toxin contains a single toxic component neglected the habitual complexity of biological products, as, for example, the mixture of related alkaloids in opium.

Arrhenius and Madsen interpreted the first two findings as indicating a mass action effect between substances of weak affinity. The Danysz phenomenon is incompatible with this view. Bordet regarded neutralization of toxin by antitoxin as an adsorption phenomenon without fixed quantitative relations. In the absence of pure preparations of the reagents, the controversy is in abeyance. But the existence of toxoid has been fully substantiated and it can be produced by the action of formaldehyde on toxin. Also, the toxin–antitoxin combination, while more or less reversible in recent mixtures, for example by dilution, becomes firm later; the toxin, however, is not destroyed by the reaction, but can be dissociated by alteration of *p*H, etc.

Side-chain theory. As mentioned above, Ehrlich regarded the molecule of protoplasm as being furnished with side-chains (later called receptors); certain of these (nutriceptors) have the function of maintaining the life of the cell by combining with food molecules. If substances such as toxins, which, as now appears, are actually proteins, in addition to being able to combine with receptors by means of their haptophore groups, also are poisonous, that is, possess a toxophore group, then the cell will be damaged. The damage may be sufficient to kill the cell, but short of this the cell will survive and may be stimulated to produce excess of similar receptors, according to Weigert's law of hypertrophy in response to functional demands. Finally, these receptors, instead of remaining attached to the cell (sessile), may become free in the circulation. Here the free receptors will combine with the specific toxin which stimulated their development and so act as antitoxins by neutralizing toxin before it reaches the cellular protoplasm. This hypothesis embodies a pharmacological principle that chemical substances

(toxin or drug) in order to act on living cells must first combine with them. As expressed by Ehrlich, "*corpora non agunt nisi fixata*". In the case of dyes, the site of fixation can be recognized by the eye; and he strove to obtain dye derivatives of alkaloids which would retain their characteristic pharmacological action, but met with little success. It is of interest that Grotthus and Draper had made a similar statement from their observations on photochemical effects.

Failure to extract antibodies in quantity from any organ or tissue has so far prevented their identification with sessile receptors; but several facts support the view. Thus, after bleeding an immunized animal at a static phase of antibody production, there is an accession of antibodies to the blood; again, the supersensitiveness of blood-free tissues in animals rendered actively anaphylactic, as well as the phenomenon of delay in establishing passive anaphylaxis, are scarcely explicable except on the basis of sessile receptors (see below). (Evidence from the use of 'markers' is omitted until more is known as to the ways in which they may be distributed in the constituents of the body.) No evidence negatives the theory. It fell into disrepute after the first rather uncritical enthusiasm for it. But now knowledge that antibodies most probably are globulins and inquiry into the sites of globulin production have caused it to be seriously considered again, and recent diagrams of the complementary coilings of protein molecules recall Ehrlich's visions of fifty years ago re-dressed according to modern chemical fashion. One objection to the theory, namely, that antigens, which are largely proteins, so far from being analogous to normal nutrients of the cells, are usually intruders into the body as infective agents or artificially introduced parenterally, has been answered by the work of Whipple. He has produced the strongest evidence that free entrance of protein to the interior of cells does occur. The high specificity of antibodies for the corresponding antigens was accounted for by Ehrlich on the supposition that a receptor pre-existed for each antigen. At present it is explained by the antigen acting as a sort of template for the pattern of the globulin antibody. This still leaves the problem unsolved as to how, like a 'paternal impression', the influence of the antigen can persist long after it has presumably disappeared.

Ehrlich recognized in Bordet's discovery of hæmolytic antisera an invaluable instrument for analysing *in vitro* both qualitatively and quantitatively the mechanism which also underlies bacteriolytic and bactericidal action; and by this means, too, he obtained further insight into the properties of receptors. Essentially, as Bordet showed, the cytolytic effect depends upon an antibody, which is specific and thermostable at 55° C., co-operating with complement (alexin), which is a non-specific constituent of normal serum and plasma, not increased by immunization and thermolabile; both act quantitatively and complement disappears in the process. The fact that the antigens of the red corpuscles reside in the stromata and so are particulate enabled absorption experiments to be carried out by Ehrlich; for example, a suspension of corpuscles freed from their native serum by repeated centrifuging with isotonic saline was added to heated antiserum and after a time the mixture was centrifuged; the supernatant was then tested for its content of antibody and likewise the sediment, after washing with saline. Cells, antisera and complements from many animal species were examined in conjunction and the temperature of the suspending fluid varied at different stages. Thus, it was found that the antibody is fixed by red cells at temperatures down to 0° C., whereas at the latter point complement is inactive in the presence of antibody and fails to be fixed. Complement is not fixed at 37° C. in the absence of antibody. Depending on the species of the red corpuscles and of the animal yielding the antibody, complement of a particular species may fail to cause lysis, that is, may be 'non-dominant'. (Muir showed afterwards that such failure may be due either to non-combination of the complement or to lack of toxicity in the particular circumstances.) Ehrlich called the hæmolytic antibody an amboceptor, since he conceived that it had two haptophore groups and so acted as a link between the receptor of the antigen and the complement, enabling the zymotoxic or ergophore (toxophore) group of the latter to attack the red cell. In the absence of conclusive evidence of its linking action, Bordet preferred to call the antibody a sensitizer. Muir, on finding that antibody alone could be dissociated from sensitized red cells which had been saturated with complement (and lysed in the process), used the term 'immune body' for an antibody which along with the corresponding antigen leads to combination of complement—which may or may not be followed by cytolytic action.

The chemical basis of specificity of receptors, rather than the biological, was emphasized by Ehrlich: this is well illustrated by the finding that a hæmolytic immune body developed in the rabbit by ox blood corpuscles also leads to lysis of sheep's corpuscles by complement; but absorption experiments show that it contains two moieties, one fixed by both species of red cells, the other only by those of the ox.

The hæmolytic agent in certain normal sera, for example that of the guinea pig for ox corpuscles, has the same double constitution. When red cells of one individual were injected into others of the same species a hæmolytic immune body developed in certain cases; this was called an isolysin. Therefore, individuals differ sufficiently to enable certain receptors of one to exert an antigenic stimulus (*ictus immunisatorius*) in others. But isolysins developed by the same blood corpuscles in different individuals can be shown by absorption experiments not to be identical. Hence the receptor apparatus of the recipient determines which receptors of the donor will act as antigens. Attempts to produce an autolysin by injecting an individual with his own blood failed. This protective mechanism, *horror autotoxicus*, as Ehrlich called it, may break down, however, as in paroxysmal hæmoglobinuria *e frigore* (where the lytic antibody unites with the red cells only when the temperature falls below 37° C.). This form of hæmoglobinuria is usually associated with syphilis. Some cases of hæmolytic anæmia, a condition which now claims much attention, are also due to autoantibodies. The nature of the derangement which brings about autolysin formation is unknown; but recently it has been shown that the presence of an 'adjuvant', such as a killed culture of tubercle bacilli, may stimulate the development of antibodies to substances which by themselves would not act as antigens.

The question whether antibodies act as antigens was partially resolved by confirming Bordet's demonstration of 'antiamboceptors' which prevent union of complement. On the other hand, the apparent

existence of anticomplements was later shown by Moreschi to be simulated by a Bordet–Gengou reaction. Thus, on injection of foreign serum, an antibody is produced; *in vitro*, this along with the serum fixes complement, the indicator being sensitized red corpuscles added later, which remain intact. The delicacy of this test for determining the species of serum and certain other proteins in amounts of the order of less than 1γ exceeds that of the precipitin reaction. The work of Neisser and Sachs on this subject in Ehrlich's laboratory emphasized its practical value, the most outstanding instance of which is the Wassermann reaction.

Theobald Smith directed attention to the observation that guinea pigs which had survived the injection of a mixture of diphtheria toxin and antitoxin from the horse became severely ill and often died when they received a large dose of horse serum at a later date. But animals which had originally received a massive dose of serum alone (to confirm absence of harmful constituents) usually withstood the second dose. Analysis of the "Theobald Smith phenomenon" by Otto in Ehrlich's laboratory and by others showed that this form of supersensitiveness, called anaphylaxis, has as its basis the antibody reaction set up by the original minute dose of foreign serum, and that it is specific and essentially independent of the toxin, although the latter may be an adjuvant. Anaphylaxis can be transferred passively. This work played a large part in emphasizing the importance of allergic phenomena in disease.

Ehrlich's 'wet nurse experiment' in mice demonstrated that transmission of antitoxic immunity to the offspring occurs only through their ingesting the milk of an immunized female, which contains the antibody—but in some species there is transplacental transfer. Thus the immunity of the young is passive. There is no hereditary transmission of acquired humoral immunity either from the father or mother.

In 1908 Ehrlich shared with Elie Metchnikoff the Nobel Prize for Medicine "in recognition of his work on Immunity".

[1] Engelhardt, A. v., "Emil von Behring", *Behringwerk-Mitteilungen*, **10** (Berlin, 1940). MacNalty, A. S., *Brit. Med. J.*, i, 668 (1954).

[2] Apolant, H., *et al.*, "Paul Ehrlich" (Jena, 1914). Marquardt, M., "Paul Ehrlich" (London, 1949). "Paul Ehrlich Centennial", *Ann. New York Acad. Sci.*, **59**, 141 (1954) (includes assessments by various authors of Ehrlich's work and present-day developments). Himmelweit, F. (ed.), "The Collected Papers of Paul Ehrlich" (London, 1954).

[3] Riley, J. F., *Lancet*, i, 841 (1954); *Nature*, **174**, 318 (1954).

(*To be continued*)

EVOLUTION OF THE EARTH

A JOINT discussion of the Geological and Royal Astronomical Societies was held in the apartments of the Geological Society at Burlington House on February 2 to consider problems discussed by the late Dr. G. M. Lees in his presidential address to the Geological Society in 1953—"The Evolution of a Shrinking Earth" (*Quart. J. Geol. Soc.*, **109**, 217–257; 1953). This address was not primarily concerned with "The Origin of the Earth", the advertised title of the discussion, and only one speaker, Mr. T. Gold, related his remarks to that problem. Unfortunately, many who came to listen—and some to speak—failed to gain a footing in the overcrowded meeting room.

Prof. L. Hawkes, in opening the discussion, said that Dr. Lees had challenged some conceptions regarding the earth's crust which are widely held by both geologists and geophysicists; in particular, his view that there may be no fundamental difference between the basement of the oceans and the continental masses could not be accepted. It has been firmly established, first by geologists and later by geophysicists, that the rocks beneath the oceans are denser than those in the upper part of the continental crust. The discovery by the seismologists of the Mohorovičić discontinuity (the 'Moho'), where lighter material overlies denser material, has given precision to the picture, and provided a convenient definition of the 'crust' as comprising the rocks above the 'Moho'. The 'Moho' is probably world-wide, and no significant difference has been found in the velocities of shock-waves in the sub-Moho material beneath the oceans and that beneath the continents. In two areas in North America, H. E. Tatel, L. H. Adams and M. A. Tuve (*Proc. Amer. Phil. Soc.*, **97**, 658–669; 1953) have failed to find the 'Moho', and it may be that in orogenic disturbances some mixing of lower crust and mantle may take place. Although the earlier conception of a continental crust composed of sharply defined horizontal layers of different density is now known to be erroneous, the term 'granitic layer' is still useful in directing attention to a feature of the continental crust which is absent or only sparingly present in the oceanic areas. The oldest rocks known include sediments transported by and laid down in water, which indicates the presence of oceans at the beginning of geological time. The difficulty in finding a satisfactory theory for the ocean–continent relationship may lie in the fact that it was established in pre-geological time and perhaps by processes which have not been operative since. There is evidence that throughout geological time there have been continents and oceans, a crust behaving under stress as it does now, igneous material with the same variable composition coming up from below, a similar temperature to that of the present, and perhaps life existing throughout. The geologist sees no vestige of a beginning. The remarkable uniformity of crustal conditions and happenings for, say, the past three thousand million years is a fact which must find a place in the speculations of the cosmologist.

Mr. T. Gold discussed the formation and internal development of an earth formed by the agglomeration of solid particles—a model more acceptable to astronomers than the scheme of an originally liquid earth. From a cloud of dust and gas, lumps of solid are formed which aggregate through collision into a large mass bearing the scars of impact, a method of growth fitting the interpretation of the lunar features. In such a model various sources of heat are available—the compression of the interior causing a temperature rise of perhaps 2,000°, the attenuation of seismic waves caused by the impacts, and radioactivity causing a gradual rise of 2,000° or 3,000° in three thousand million years. During growth and afterwards, this heating causes a certain amount of melting; everywhere liquid will be mixed with solid long before complete melting could occur. A structure of pores or veins of liquid results, and a transport of liquid depending upon density may occur. The core

of the earth may have arisen in this way by the downward percolation of dense liquid—molten iron or other substances metallic at the pressures. Lighter liquid penetrating upwards may have supplied the atmosphere, the oceans and the crust. The transport of liquid upwards being prevented by the lower temperature of the crust ('thermal blockage'), vulcanism is only possible where there are fractures sufficiently large to alter the thermal structure. Quickly changing stresses resulting from the percolation of liquid from one level to another give rise to earthquakes, a series of shocks rather than single events being the rule. The same type of process is considered responsible for the major deformations of the crust. The internal flow and hydraulic actions to be expected from the model give new freedom for explaining the major problems of earth structure and movement.

Prof. C. E. Tilley commented that, although cosmology is not the province of the geologist, he has a right to express a view as to how matter in the deeper crust and upper mantle is likely to be organized if the earth had passed through the liquid state, and to discuss the implication of Mr. Gold's model. Mr. Gold would have difficulty in explaining the gross layering of the earth's interior without assuming extensive fractional melting. Geologists have been unable to accept the geophysical concept of sharply defined upper and intermediate layers of the crust, and it is reassuring, he said, to have the pronouncement of H. E. Tatel, L. H. Adams and M. A. Tuve that the crust above the 'Moho' in North America may be about as irregular and inhomogeneous as the rocks exposed in the Basement Complex area. In the Canadian Shield, Dr. Lees had estimated thicknesses of at least 200,000 ft. involved in tectonic belts—much exceeding the accepted crustal layer of 40 km.—yet the 'Moho' had been found at that depth in Minnesota. The 'Moho' could reasonably be associated with a change to ultra-basic material of peridotitic composition. Occurrences of peridotite at St. Paul's Rocks on the mid-Atlantic Ridge, dredged samples of serpentine from south-west of the Azores, and the bastite serpentine 'in place' on the Gettysburg Bank between Gibraltar and the Azores are of significance in ocean areas where the 'Moho' is at a relatively shallow depth. Is it not probable, Prof. Tilley asked, that the mylonized peridotite of St. Paul's Rocks is a fragment from beneath the 'Moho' brought up in a great line of fracture? Recent measurements of heat flow under the oceans have emphasized our lack of knowledge of the radioactivity of oceanic rocks. Petrology and geochemistry, through their recently developed experimental techniques, could contribute in increasing measure to the common problems of geology and geophysics.

Sir Edward Bullard said we cannot at present explain even in principle how the earth has developed to its present state, and that what matters in a synthesis is not whether its details will prove correct but whether it relates the known facts in a way that suggests fresh investigations and experiments. The needs of the petrologists, the measurers of gravity and the seismologists are reconciled in the present accepted picture. The 'granitic layer' of the seismologists can be equated with the 'basement complex' of the Pre-Cambrian and the 'intermediate layer' softened to a gradual and regionally variable increase in the proportion of basic rocks with depth. It seems likely that the 'Moho' represents a boundary below which the complications of surface geology do not extend. The 'Moho' must represent a change of material and not a phase change, since the pressures and temperatures concerned are within the range accessible to laboratory experiment, and such a conspicuous change in a common type of rock could scarcely have escaped attention. The behaviour of continental structures at the boundary to the ocean is of critical importance. Dr. Lees assumed that the structures continued out to sea and that the continental rocks must likewise continue. It seems unlikely, Sir Edward said, that the forces which produced a mountain range on the continent would have stopped short sharply at its edge. It does not follow, however, that the continental rocks continue beyond the edge; the material on which the mountain-building forces act may be different, and continental features usually have no topographic continuation on the floor of the deep sea—as can be seen, for example, from the Hercynian mountains of Europe and the extension of the Appalachians across Newfoundland.

In the open discussion following the four principal contributions, Sir Harold Jeffreys, commenting on a criticism in Dr. Lees's address, said that mathematics is as much a tool as the geologist's hammer or microscope. It tests whether suggested explanations do explain, and it has the property that its methods are always open to inspection. There is no satisfactory ground for believing that the folding measured in mountains is identical with the crustal shortening. Mr. M. W. Strong directed attention to the amount of folding that can be accounted for by local rearrangement of rock masses associated with batholithic intrusions rising and thrusting the sedimentaries aside much in the manner of a salt-plug, but on a vaster scale. Prof. R. M. Shackleton also questioned Dr. Lees's inference of immense crustal compression. Although the oldest visible rocks generally dip at high angles, it does not follow that the crust has suffered general compression. Some of the oldest parts of the crust, for example Southern Rhodesia, show structures primarily due to the rise of granite plutons between which sediments have been sucked down.

Summing up the discussion, Prof. O. T. Jones referred to the view that a continental layer of 35–40 km. could not accommodate in their visibly crumpled form the vast thicknesses of sediments in certain regions, and he pointed out that the effect of one period of diastrophism might have been obliterated before the beginning of the next period of deposition. What remained is a small fraction of that originally laid down and may thus be accommodated without assuming an excessive thickness of crust. It is difficult to arrive at an estimate of the total shrinkage of the earth from the continental areas alone. Mr. Gold's model of a sponge-like interior of rock and metal, he said, does not bear any close relation to any earth with which the geologist is familiar. It does not seem to explain the separation of oceanic and continental areas, nor does it seem to account for the long narrow belts of crumpled strata arising from compression at various times. Although it is said to account for volcanic activity in providing a source of molten material near to the surface at any time, it does not provide an explanation of the long belts along which volcanoes are strung out. The discussion had been of value, however, in the pooling of ideas and in emphasizing the need for new evidence regarding the earth's interior and behaviour and for more accurate data on the properties and materials of the earth's crust.

L. Hawkes

OBITUARIES

Sir Charles Martin, C.M.G., F.R.S.

CHARLES JAMES MARTIN was born in London in 1866. He received his early education privately and later entered King's College, London, before going to St. Thomas's Hospital, where he qualified in medicine. He was a brilliant student, winning many distinctions, and was a gold medallist and University scholar in physiology. For a time he studied at the University of Leipzig under Karl Ludwig. Shortly after qualification, in 1891, he went out to Australia and after holding junior posts in the departments of physiology at Sydney and Melbourne, became professor of physiology at Melbourne in 1901—the year in which he was elected to the fellowship of the Royal Society.

His work over a period of twelve years in Australia not only showed that he was a potential research worker of great ability but also a man who could inspire and initiate work in varied fields. He exerted a great influence on medical education and is acknowledged as one of the founders of medical research in that country.

In 1903 Martin returned to England to become the director of the Lister Institute of Preventive Medicine. He had such a profound influence upon the development of the Institute that he may be said to have created it and was largely responsible for the high quality of its scientific work and the large number of scientists who were trained during his directorship.

In the interruption caused by the First World War, he joined the Australian Army Medical Corps and received the rank of lieutenant-colonel. He organized the laboratory pathological services for the Gallipoli campaign and dealt with the difficulties connected with amœbic and bacillary dysenteries and the typhoid fevers. This work was later continued in Egypt and Palestine. In 1917 he went to France, where he organized and directed the pathological department for the 23rd General Hospital of the British Royal Army Medical Corps at Rouen. He was twice mentioned in dispatches and was made C.M.G. for his war service.

When, in 1930, he retired from the directorship of the Lister Institute, he accepted the invitation of the Australian Council of Scientific and Industrial Research to take temporary control of the Institute of Animal Nutrition at the University of Adelaide, where he was appointed professor of biochemistry and general physiology. Returning to England after three years, he was still active in many scientific fields. While living in retirement at Cambridge he carried out a fundamental research on myxomatosis of rabbits and its immunological implications. In collaboration with colleagues at the Lister Institute in London, he took an active part in an experimental study of the nutritive value of maize, made on pigs at Cambridge, as a contribution to the solution of the pellagra problem in man. On the outbreak of the Second World War, he arranged accommodation at his house in Cambridge for the Nutrition Unit which was evacuated from the Lister Institute in London, and gave valued help to the various war problems which devolved on this team. The war over, Sir Charles was seventy-nine years of age; it was only then that the disabilities of old age began to tell upon him. Even so, in the following years he carried on with scientific work—his last paper was published in 1948—and was able to make useful comment upon the work of those colleagues who came to see him, and to keep to the end his interest in scientific matters. He was chairman of the Committee of the Dunn Nutrition Laboratory in Cambridge until 1946 and scientific adviser to the International Wool Secretariat until 1949. He died on February 15, in his ninetieth year.

Martin's achievements lay in many different fields of scientific inquiry. In his early days in Australia, he was concerned with problems of the metabolism and the heat exchange of marsupials and the monotremes *Echidna* and *Ornithorhynchus* (duck-billed platypus), those 'half-mammals' indigenous to that country. Added to this work were studies of the toxins and antitoxins of snake venom, in the course of which he developed an ingenious ultrafilter, thereby demonstrating the difference in their molecular sizes. While at the Lister Institute, his own researches included studies on the epidemiology of plague and the mechanism by which the infected rat flea is enabled to infect the human host, and the mechanics of the disinfection process and of the heat coagulation and precipitation of proteins. With himself as subject, he investigated the thermal exchange and heat regulation of the human body under varying conditions of environment and physical work. His lectures on this subject were delivered as the Croonian Lectures of the Royal College of Physicians in 1930. He took an early interest in the modern study of nutrition, and from 1910 onwards work was in train at the Institute on the cause of beriberi and the distribution among foods of the preventive vitamin. A prepared mind thus enabled him, in 1915, to recognize, as a form of beriberi, a disorder among the Australian troops in the Middle East which had baffled the Army clinicians, and to recommend measures for its prevention and cure. After the end of the First World War he became interested in the biological value of food proteins and, again on his own person, carried out experiments which are acknowledged as a model for tests of this type.

In addition, he was an inspiration to his colleagues who dealt so successfully with the problems of fermentation, calcification of bone, the chemistry and metabolism of fat, plague, immunology, bacteriology and nutrition. Though he was not trained in all the necessary techniques, he was widely read, had an excellent memory and could contribute usefully to work in many varied fields. He was able to see the essence of a problem and to sense the lines upon which its solution might be possible. This, coupled with his ability to make apparatus that would do the job both for himself and for others, made him so valuable in the early days in Australia where equipment was lacking, and at the Lister when by far the quickest way to get apparatus was to make it oneself.

Although Martin left Australia when he was thirty-seven years of age, he never lost his contact with that country, a contact enlivened by the constant stream of Australian graduates who came to the Lister Institute. There they found a spirit of intellectual adventure which was kept in proper bounds by severe criticism, hatred of slipshod work, great integrity and dislike of self-advancement. Australia never ceased to appreciate what he had done, and in 1952 the Australian Government founded two medical research fellowships in his name to enable young Australian scientists to work overseas.

Sir Charles Martin received the Royal Medal of the Royal Society in 1923. He was a doctor of science of the Universities of London and Melbourne and held honorary doctorates of the Universities of Sheffield, Edinburgh, Durham and Trinity College, Dublin, and was an honorary M.A. of Cambridge. He was knighted in 1927. In 1926 he was made a member of the Medical Research Council, and he gave valuable help on many government committees.

Sir Charles Martin married Edythe, daughter of Alfred Cross, of Hastings, and had one daughter. His wife died in March 1954, at the age of ninety-four years.

Harriette Chick
Alan N. Drury

It was in his capacity as chairman during 1934–46 of the Committee of the Dunn Nutritional Laboratory, Cambridge, that I had the privilege of getting to know Sir Charles Martin well, and so of coming to respect, to admire and to love him. Intellectually, what stood out most was his astonishing width of interest and knowledge, in the most varied fields of medical research. Equally at home in many specialized departments of pathology, physiology, bacteriology, or biochemistry, he had the gift of seeing right into the heart of a problem; and knowing, as he did, how the present knowledge had been won, he quickly sensed what gaps still remained to be filled in. He was interested in knowledge for its own sake, and, unlike some lesser men, judged a research finding on its merits alone, not by its authorship. In consequence, he was able to recognize talent and originality where others might miss seeing it, and, as a result, had the satisfaction of fostering young, and sometimes precarious, research careers—leading in one instance at least to a later Nobel laureateship. He was never one of those prone to put his own name on the title of the papers of his assistants and students, published from his institute. On the contrary, it was an open secret that, during the years that he was director of the Lister Institute, much of the now classical work appearing under other names was really suggested, inspired and directed—sometimes even down to the smallest technical details—by him. He himself took a pride in being a competent technician and handyman, and in "Who's Who" gave "tinkering" as his hobby. Entirely devoid of affectation and pretentiousness, he had not the inclination to waste time, for example, on the elegancies of dress, and on more than one occasion had—but only for a moment—been mistaken for a wandering tramp.

Martin's scientific integrity was marked by a robust sense of right and wrong, and fair dealing, combined with practical common sense. He was prepared, in no uncertain voice, when occasion demanded, to stand up against established authority. To his junior colleagues and to his friends, he could at times be blunt and outspoken to a degree; but his direct speech never caused resentment, and one was warmed by the friendly, welcoming smile, always lurking below. Although in his own tastes simple to a degree, he could prove himself a man of the world in dealing with officialdom; indeed, one of his maxims was that people who failed to rub shoulders with their contemporaries had not succeeded in learning one of the elementary 'techniques' of their trade. Another of his maxims was that it is useless to appeal to reason where a person's emotions have become involved. Up to the end, Sir Charles retained both his charm and penetrating intellectual faculty.

Leslie J. Harris

Dr. W. W. Barkas

Wilfrid Watson Barkas, reader in paper-making technology in the Faculty of Technology of the University of Manchester, died on January 30 at the age of fifty-seven. Dr. Barkas was a Northcountryman who was educated at the Friends' School in Kendal and in the University of Manchester.

During the latter part of the First World War, Barkas served with the Friends' Relief Service in France and returned home with "a deep appreciation of the finest qualities of the French peasant" and "a love of French food and wine". After graduation in physics and mathematics in Manchester, he took a teacher's diploma; but he was glad that he did not become a teacher. Instead, he joined the staff of the Physics Department of University College, London. He never fully recovered from a serious illness he had at this time.

In 1930 he was appointed to organize the Timber Physics Department at the Forest Products Research Laboratory in Princes Risborough, where he proved a "generous and inspiring leader". While there he published a considerable amount of original work on the properties of fibres and fibre assemblages, for which he obtained his D.Sc. in 1945 and his fellowship of the Institute of Physics in 1946.

In 1949 he took charge of the Paper Making Section in the Manchester College of Technology, where he completely re-organized the courses. In doing this he was helped by his good personal relations with the leaders of the paper and board industry, who showed their support of him by the foundation of the George Rackley Scholarships to encourage students to take the new courses.

Barkas's research work greatly impressed foreign scientists. In 1948 he was invited to deliver a series of lectures at the Swedish Forest Products Research Laboratory. These lectures were very well received and Prof. Steenberg says of them that they have had "a very marked influence on the general way of thinking in Scandinavia". Last autumn there was a symposium at the Institute of Paper Chemistry in Appleton, Wisconsin, sponsored by the Research Councils of the Technical Association of the Pulp and Paper Industry of the United States and the Canadian Pulp and Paper Association and attended by two hundred of the leading workers in this field. As Dr. Barkas himself was not able to attend, the delegates to the symposium sent him a cable of appreciation of his work on which so much of their discussion had been based.

It is very sad that he did not live to see the full fruition of his ideas. He will be greatly missed by all who knew him.

J. M. Preston

Dr. C. W. Bellerby

Charles William Bellerby, who died on October 27 last year, will be remembered for several noteworthy contributions to reproductive endocrinology. He graduated in 1923 in Cambridge, as a member of Christ's College, and in 1925 joined me in the Department of Physiology in University College,

London, where we carried out a series of researches on ovarian extracts. Later he spent some time with Prof. J. (afterwards Sir Jack) Drummond in the Department of Biochemistry, and with Dr. F. H. A. Marshall in the School of Agriculture, Cambridge. During this period he made the observation that the œstrous rabbit could be caused to ovulate by the administration of anterior pituitary extracts. In 1934 he was awarded a Beit Fellowship to work with Prof. L. T. Hogben at the London School of Economics and made valuable contributions to the study of *Xenopus laevis* as a laboratory animal and to its use for pregnancy diagnosis. During the Second World War he was concerned with civil defence and operational research, and afterwards with archæological investigations.

A. S. PARKES

NEWS and VIEWS

Sir Edward Bullard, F.R.S.

SIR EDWARD BULLARD'S decision to resign from the directorship of the National Physical Laboratory and to accept a research fellowship at Gonville and Caius College, Cambridge, may have surprised those unfamiliar with his earlier career. Ever since 1934, when he became University demonstrator in the Department of Geodesy and Geophysics at Cambridge, his interests have centred around the earth sciences. Apart from the War years, he remained at Cambridge until 1948, during which time he not only made important contributions to these subjects himself but also stimulated others to study geophysics. As professor of physics at Toronto (1948–49) he built up a school which now trains nearly a quarter of all the geophysicists in North America. It is natural, therefore, that, after five years at the National Physical Laboratory, Bullard should wish to go back to Cambridge to devote himself to geophysics. His return will be welcomed by all those interested in the development of the earth sciences in Britain. The numbers of geophysicists trained each year in Great Britain is only about one-twentieth of the number in the United States and is inadequate to meet the rapidly growing needs throughout the Commonwealth. Bullard's return to Cambridge may well lead to an increase in teaching and research, and so help to raise both the quantity and quality of British geophysicists.

Geology at Cambridge : Prof. W. B. R. King, O.B.E., F.R.S.

PROF. W. B. R. KING retires from the Woodwardian chair of geology at Cambridge at the end of this academic session. As a graduate of Jesus College, a Fellow of Magdalene, a member of the Sedgwick Museum's teaching staff in the inter-war years, and professor since 1943, he has had a long association with Cambridge geology ; but he has also held other appointments which have given him a great width of experience. In chronological order may be mentioned his period as a member of the Geological Survey, his service as an army geologist in France during the First World War, his tenure of the chair at University College, London, and his distinguished services for the army during and after the Second World War. At present he is completing his second year as president of the Geological Society of London. Prof. King's research work has had the variety which his career might suggest. It has ranged from the stratigraphy of the Lower Palæozoics of Central Wales and Northern England to that of the Pleistocene of the Thames and East Anglia, and from the geomorphology of his native north-west Yorkshire to the hydrology of the Chalk. In recent years, working in close collaboration with the Admiralty and the geophysicists, he has become the recognized authority on the geology of the English Channel. He retires full of vigour and with the leisure to increase his reputation as a research geologist.

Dr. O. M. B. Bulman, F.R.S.

DR. O. M. B. BULMAN, who will succeed Prof. King, is one of the best known of the students of Prof. W. W. Watts at the Imperial College of Science and Technology, London. He proceeded afterwards to Sidney Sussex College, Cambridge, to study for his Ph.D. degree, and, after a short break, returned to Cambridge as a member of the Sedgwick Museum. When Dr. Henry Woods retired, he became reader in palæozoology, and it is from this position that he has been elected. Although Dr. Bulman's election breaks a long sequence of stratigraphers in the Woodwardian chair, he is no stranger to stratigraphical research, while the special side of palæontology which he has made so much his own is the most-valued of tools in the stratigraphers' hands. It is, however, as a pure palæontologist, and in particular as a student of the graptolites, that Dr. Bulman has established his world-wide reputation. He stands now as the rightful wearer of the mantle which Lapworth first assumed.

Meldola Medal, 1954

THE Meldola Medal is the gift of the Society of Maccabæans and, on the recommendation of the Council of the Royal Institute of Chemistry, is awarded each year to a British chemist less than thirty years of age on the strength of his or her published work. This year it has been awarded to Dr. J. S. Rowlinson, lecturer in chemistry in the University of Manchester. Dr. Rowlinson is a graduate of the University of Oxford, where he took his doctorate for research on some of the physical properties of organic vapours, particularly the dispersion of ultrasonic waves in gases. On going to Manchester in 1951 he extended his work on liquids to regular solutions and also studied the surprisingly high solubility of solids in compressed gases, which was shown to be due to forces in the gas-phase between single molecules of the solid and clusters of molecules of the gas. Dr. Rowlinson has recently been developing a perturbation treatment of the effect of molecular shape on the bulk properties of fluids, and is also doing experimental work on the properties of liquids and compressed gases, using highly polar substances, fluorine compounds and iodine solutions.

Iron and Steel Institute

THE following awards have been made by the Iron and Steel Institute : *Bessemer Medal* (1955), to Prof. John Chipman, head of the Department of Metallurgy, Massachusetts Institute of Technology, in recognition of his distinguished contributions to the knowledge

of the physical chemistry of steel-making; *Sir Robert Hadfield Medal* (1955), to Mr. Tor Fjalar Holmberg, of Oy Vuoksenniska A.B., in appreciation of his meritorious service in improving the technique of the production of iron and steel at the Imatra Works, Finland; *Andrew Carnegie Silver Medal* (1954), to Mr. B. Cina for his paper on the effect of cold work on the gamma–alpha transformation in some iron–nickel–chromium alloys (*J. Iron and Steel Inst.*, **177**, 406; 1954); *Williams Prizes* (1954), of £100 each, to W. Jackson for his paper on the use of cold coke oven gas and pitch–creosote firing in tilting furnaces (*J.*, **178**, 378; 1954), R. McDonald for his paper on steelworks waste-heat boiler practice (*J.*, **176**, 71; 1954), and A. Stirling for his paper on the pelletizing of Northampton sand ironstones by vacuum extrusion (*J.*, **177**, 25; 1954).

Diploma of Fellowship of the City and Guilds of London Institute

The Council of the City and Guilds of London Institute has conferred the diploma of fellowship upon the following past students of the City and Guilds College: Mr. A. McL. Mooney, deputy director of electrical engineering, Admiralty, a post in which he has been responsible for much special development work; Sir Ralph Reed, lately chairman of Albert E. Reed and Co., Ltd., paper manufacturers, who was paper controller for the Government during the Second World War; Dr. E. H. Rodd, formerly of the Dyestuffs Division, Imperial Chemical Industries, Ltd., whose work in the dyestuffs industry has been responsible for many advancements, both in fundamental knowledge and in industrial practice; Mr. N. E. Rowe, technical director of Blackburn and General Aircraft, Ltd., formerly of the Ministry of Aircraft Production, and now president-elect of the Royal Aeronautical Society; Mr. C. W. Speirs, formerly of the Morgan Crucible Co., Ltd., London, and a pioneer in the application of carbon in the electrical industry.

Training of Engineers

A new method of training boys leaving public and grammar schools to become professional engineers capable of filling responsible engineering, administrative and sales positions in industry has recently been introduced by the General Electric Co., Ltd. It is an industry-based 'sandwich scheme' operated by the Company in conjunction with the Birmingham College of Technology. In future all boys selected by the Company for this training will, on leaving school at the age of eighteen, be given a five-year course, in which full-time sessions of six months at the College of Technology will alternate with six-month periods of industrial training in the Company's works. At the end of the course a young man will have gained exemption from the professional requirements of a body such as the Institution of Electrical Engineers, and will, if he remains with the Company have as good prospects in the Company as the man who has spent three years at the university followed by two years as a graduate apprentice. During the whole of the five-year course, the Company not only pays a student's college fees but also gives him suitable remuneration to cover his living expenses. Two country houses in the Midlands are used by the Company as halls of residence. Boys on the course have their national service deferred until its completion. The college and industrial elements of the course are planned as a whole and are sufficiently flexible to meet the needs of individual students. At the moment about sixty boys at the Birmingham College of Technology are Company student trainees on the first year of their course. In three years time this number will have risen to between 250 and 300.

Queen Elizabeth House: Oxford Centre for Commonwealth Studies

A charter has now been granted by H.M. the Queen to Queen Elizabeth House, Oxford, the new Oxford centre for Commonwealth studies, and in it the purpose of the foundation is defined as follows: to facilitate studies in political, economic, legal, administrative, social and cultural matters affecting the peoples of the British Commonwealth overseas and especially, but not exclusively, the peoples of the Colonies, Protectorates and other territories for which the Government in Britain is directly responsible; to provide a centre to which persons of authority or influence can resort for the study of such matters and the exchange of information; to assist such persons to obtain access to the academic resources of Oxford and elsewhere; and generally to act as a link between individuals and institutions concerned with these affairs. It will be noted that, when the project was first announced (see *Nature*, **174**, 19; 1954), Queen Elizabeth House was to be a centre for Colonial studies, but that this has now been broadened to include Commonwealth studies generally, though the Colonial aspect is still the prime one. The Government has appointed Viscount Chandos as president of the governing body of Queen Elizabeth House, which will consist also of the vice-chancellor of the University of Oxford *ex officio*, four members appointed by the Government, four appointed by the University of Oxford and not more than eight appointed jointly by the Government and the University. The names of most of the members have been announced. Subject to confirmation, temporary quarters for the House have been secured in St. Giles, Oxford.

Abstracts of Instrument Techniques

The one hundred and fourth issue of the *Bulletin of the British Scientific Instrument Research Association* (9, No. 11; November 1954) contains the twenty-thousandth abstract, compiled by the Association, of literature about scientific instruments published during the past nine and a half years, and gives an indication of the growth in importance of the science of instrumentation. The index to Vol. 8 (1953) of the *Bulletin*, which is now available, consists of an author and subject index to the 2,769 abstracts published during 1953 and covers some three hundred pages. Members of the Association and non-member organizations and individuals engaged in branches of industry or research where it is important to keep abreast of new developments in instruments, techniques and methods of measurement will find the *Bulletin* most valuable for handy reference and as an informative guide to the literature.

Meeting in New Mexico on Problems of Arid Lands

The American Association for the Advancement of Science is arranging an international meeting on "Arid Lands", to be held in New Mexico during April 26–May 4. The programme will consist of a symposium, on "What is the Future of Arid Lands?", during April 26–29 in the University of New Mexico, Albuquerque, at which there will be a discussion

meeting on the final day preceded by four technical sessions as follows: variability and predictability of water supply in arid regions; better use of present resources; prospects for additional water sources; and the better adaptation of plants and animals to arid conditions. Following this there will be a two-day field trip, and then a conference will be held during May 2–4 at the New Mexico Institute of Mining and Technology, Socorro, New Mexico. At this conference a specially invited group of experts, including members of the Unesco Advisory Committee on Arid Zone Research, will discuss the points raised at the symposium and try to formulate some definite recommendations for research and development programmes in the near future. Further information can be obtained from the American Association at 1515 Massachusetts Avenue, N.W., Washington 5, D.C.

University of London

Prof. H. R. Robinson, emeritus professor of physics in Queen Mary College, London, has been re-elected vice-chancellor of the University of London for the academic year 1955–56.

The following appointments have been made in the University of London: Dr. D. W. G. Style, reader in chemistry in King's College, to the University chair of chemistry tenable at that College; Dr. H. F. Cook, senior lecturer in the Middlesex Hospital Medical School, to the University readership in physics tenable at that School; and Mr. S. S. Frere, lecturer in archæology in the University of Manchester, to the University readership in the archæology of the Roman provinces tenable at the Institute of Archæology.

The Queen's University of Belfast

The following appointments have recently been made: Prof. P. L. Burns, professor of electrical engineering; Prof. T. P. Allen, professor of light electrical engineering; Prof. F. V. Warnock, professor of mechanical engineering. Prof. Burns and Prof. Warnock were formerly professors, and Mr. Allen lecturer, in the Belfast Municipal College of Technology.

The following lecturers have been appointed: N. R. Knowles and J. G. Murray (agricultural bacteriology); J. Lowe, R. H. Stewart and Mrs. H. Dales (agricultural botany); J. S. V. McAllister and Dr. W. O. Brown (agricultural chemistry); R. J. Willis (agricultural zoology); E. L. Calvert (mycology and plant pathology); Dr. D. Luke and Dr. J. K. L. Pearson (veterinary science).

The University announces the following grants: 16,500 dollars from the Rockefeller Foundation to be used mainly to purchase an infra-red spectrophotometer for the Department of Chemistry; £800 from the British Petroleum Co., Ltd., to provide a research fellowship in physical and inorganic chemistry; £500 from the Shell Oil Co., Ltd., to be used for research purposes in chemistry.

Announcements

Sir Harold Spencer Jones, Astronomer Royal, and Prof. S. A. Waksman, professor of microbiology in Rutgers University, New Brunswick, have been elected foreign associates of the Paris Academy of Sciences.

Mr. H. N. Ridley has been awarded the Colwyn Medal of the Institution of the Rubber Industry and also elected to honorary fellowship of the Institution in recognition of his outstanding services to the rubber industry. Mr. Ridley was the pioneer in the tapping of the rubber tree, and his hundredth birthday falls later this year. The Institution is devoting an issue of its *Proceedings* to an appreciation of his work and to tributes to his high achievements.

Mr. A. Holroyd, sewage works manager, Wolverhampton, has been appointed a member of the Water Pollution Research Board of the Department of Scientific and Industrial Research, in succession to Dr. F. S. Jenkins, who has completed his term of office.

The Arnold Gerstenberg Studentship for 1956 is open to students in the University of Cambridge who, going into residence not earlier than 1950, have obtained honours in the Natural Sciences Tripos and who wish to pursue a course of philosophical study. The Studentship will be awarded for an essay which must be submitted before May 1, 1956. Further details can be obtained from Prof. R. B. Braithwaite, King's College, Cambridge.

The tenth annual exhibition organized by the Northern Division of the Institution of Electronics will be held in the College of Technology, Sackville Street, Manchester 1, during July 14–20 (10 a.m.–10 p.m.; except July 14, 2–10 p.m., and July 16, 10 a.m.–6 p.m.). The exhibition will consist of a manufacturers' section and a scientific and industrial research section, as well as lectures and film shows. Programmes of the lectures and film shows (4½*d.*) and catalogues (2*s.*) will be available later. Admission tickets, free of charge, can be obtained from the honorary exhibition organizing secretary, Mr. W. Birtwistle, 78 Shaw Road, Rochdale, Lancs, or from any of the exhibitors.

A one-day conference on "The Film in Chemical Engineering", organized by the British Universities Film Council, in co-operation with the Shell Film Unit and Prof. G. F. Mucklow, of the Department of Mechanical Engineering, Birmingham, will be held in the University of Birmingham on April 5. Prof. F. H. Garner, of the Department of Chemical Engineering, Birmingham, and Mr. E. le Q. Herbert, of the Shell Film Unit, will be the principal speakers. The conference will be open to all. Further information can be obtained from Dr. J. Horne, University, Birmingham 15.

A symposium on "Sound and Vibration in Solids", organized by the Fachausschuss Akustik der Deutschen Physikalischen Gesellschaften in collaboration with the Fachgruppe Schwingungstechnik im Verein Deutscher Ingenieure will be held in the Mathematical Institute of the University of Göttingen during April 19–22. Twenty-five papers will be read by German workers, and the rest will be as follows: British and Italian, three each; Belgian, French and Swiss, one each. During the symposium there will be a small exhibition of industrial measuring apparatus for structure-borne sound. The fee for the symposium is D.M. 15. Further information can be obtained from "Körperschalltagung", Göttingen, Bürgerstrasse 42.

In a note in *Nature* of March 5, p. 412, it was stated that the principal contributions to a symposium on "Mechanisms of Microbial Pathogenicity" during the annual meeting of the Society for General Microbiology will be available in book form. This is being published by the Cambridge University Press, from which non-members of the Society can obtain copies (price 25*s.*).

BEHAVIOUR OF THE LIVING CELL

THE papers presented at a conference on "Tissue Culture in Pharmacology" held by the Section of Biology of the New York Academy of Sciences, and the Tissue Culture Association, Duke University, during January 14–16, 1954, have now been published (*Ann. New York Acad. Sci.*, **58** (7), 971–1326; 1954). They are concerned with the behaviour of the living cell as a whole, and contain many excellent high-power photomicrographs of living cytoplasm. Parts taken from ciné films show the motion of the various elements in the cytoplasm which is so striking a feature of living cells, not only in tissue culture but also in the whole animal, as the window technique of Algire recently demonstrated. It provides a refreshing and welcome balance in the field of cytology, which has tended to become overloaded with studies on dead cells and particularly with observations exclusively on the nucleus.

A great deal of cytology in the past has been done using fixation methods which dissolve away the cytoplasm so as to render the nucleus more accessible to observation. Since a large part of scientific thought is unconscious—and especially creative thought based on processes of which we are not aware—and since effective intuitive ideas can only be based on past experience (which may be forgotten), the process of looking at cells which have been deprived of their cytoplasm by fixation year after year would tend to create the feeling or intuition that 'there is no cytoplasm'. This is very evident in the writings of some who have subjected themselves to this activity. The papers in this collection help to remind us that cytoplasm plays a striking part in the activities of cells.

For some, the development of tissue culture over the past fifty years has been somewhat of a disappointment. The early promise in the days of Harrison and Carrel led one to expect that many fascinating experiments on living cells would be carried out. These did not appear to any large extent (with some important exceptions), and it was as if the success in getting cells to grow at all was the occasion of so much joy that progress became fixed at that point. The present series of papers represents a departure from this, and one is entertained by some of the advances in the past few years in which the cultured cell is used as a tool for discovering the answers to questions which one has been wanting to know.

Important advances in culture technique are described by W. R. Earle, G. O. Gey and their colleagues. By a systematic study of the effect of various supporting surfaces for the cells, and of agitating the medium, Earle has succeeded in regularly growing a mass of cells of the order of 1 gm. in weight from each inoculation, and, if necessary (after conditioning the medium), from a single cell. This should have repercussions in several directions, especially in biochemistry, where the use of homogeneous populations of tissue cells, instead of mixtures as heretofore, to compare cell with cell should initiate a new biochemistry of the tissue cell and, especially, a biochemistry of cancer.

The development of completely liquid media by Gey and by Earle enables cell suspensions to be handled like solutions, and measured out in aliquots, thus eliminating some of the biological variation in the testing of drugs. These liquid media also enable growth to be measured by the counting of nuclei instead of by the erstwhile indirect method of nucleic acid determination.

It is pleasing to note that the culture of cells appears to have been stripped of much of the semi-mystic ritual of Carrel and placed on a fairly scientific basis. There seems no reason why these advances in technique should not have been made thirty years ago, except perhaps a paralysing belief in the need for following a prescribed ritual.

C. M. Pomerat has measured the toxic concentrations of 110 substances on chick and human cultured cells. In view of the known wide differences in susceptibility of various mammalian species to the same drugs, and particularly to carcinogens, and the paucity of information on human material, this method should fill a gap in knowledge without the use of human volunteers and with less variation than with the use of individuals.

The use of tissue culture in the rapid screening of anti-cancer substances is reported in several papers. Here again, the importance of being able to cultivate any kind of tissue cell is emphasized. It is not yet known whether this is possible, and perhaps all the problems are not yet solved. But a favourable therapeutic index obtained on comparing the response to a drug of neoplastic cells with that of fibroblasts has sometimes given disappointing results when the drug is tested in the whole animal, where the more susceptible (but less easily cultured) intestinal epithelium and bone marrow are usually injured. As pointed out in the discussion, it would be better to use these two tissues as controls in culture.

J. T. Syverton and W. F. Scherer describe the use of cultured mammalian cells for the assay of viruses and their antibodies. Here again one notes the use of the more readily proliferating tumour cells as indicator, rather than normal cells, though the results appear to be satisfactory.

Several interesting papers describe the effects of various substances on the cytoplasm of cultured cells. While no explanations are yet forthcoming for these effects in terms of chemistry and physics, it is to be hoped that, by supplementing the observations on the more easily handled Protozoa, the comparison should bear fruit.

Pomerat and Gey re-focus attention on the important phenomenon of 'pinocytosis' whereby proteins may enter living cells. This has been almost entirely neglected since first described by W. H. Lewis in 1931. W. R. Duryee and J. K. Doherty, and also Pomerat, describe the excretion of visible material from the nucleus into the cytoplasm. The former put forward an interesting theory of mitosis.

While it is not possible to mention all the remarkable findings reported in this conference, many of the contributors seem to be conscious of the effectiveness of their approach and of the impact which it is making on the field: "Gone for ever . . . is the notion of the fixed rigidity of cells". "What greater contribution could there be to the study of the mechanism of drug action than to pinpoint with precision the part of a cell that may become altered by the drug? This qualitative approach . . . is more fruitful than the knowledge, for example, that

50 per cent of a population of cells is destroyed by a given concentration of a drug", to quote a few of the enthusiasts.

It is not the function of this survey to direct attention to misprints and the like; but the statement on p. 1224 that DNA is the chief chemical component of enzymes seems remarkable.

This report can be thoroughly recommended to biologists and pharmacologists as providing stimulating reading: so much so that it ends with a poem expressing the excitement one may feel at beholding Pomerat's ciné films. R. J. GOLDACRE

EUROPEAN ASSOCIATION OF EXPLORATION GEOPHYSICISTS

MEETING AT THE HAGUE

THE seventh meeting of the European Association of Exploration Geophysicists was held at The Hague during December 8–10, 1954, this being the first occasion when an earlier venue had been revisited. In the three years since the inaugural meeting there, the membership has grown from its anticipated strength of about one hundred and fifty to a present strength of more than eight hundred—an indication of the very active European interest in exploration geophysics. With the president, J. Goguel, in the chair, the proceedings began with a short business meeting and an opening address by Prof. Vening Meinesz. The technical meeting included the presentation of twenty-two papers, nine dealing with seismic, seven with gravity, three with electrical and three with magnetic methods. This distribution does not fully correspond with that of exploration effort between the various methods which, in terms of numbers of field parties, has been quoted recently by Germain-Jones[1] as seismic 50, gravity 18, electrical 24 and magnetic 8 per cent, out of a total of some two hundred and thirty parties based on Europe.

Four of the seismic papers described theoretical approaches to field problems, the first by Y. d'Erceville (France), dealing with the velocity of propagation of longitudinal waves in muds. The observed velocity in such materials is often lower than that of either the solid or liquid constituent, and using a simple mathematical model he showed that such a velocity might be expected. Unfortunately, the theory also predicts a velocity, intermediate between those of the constituents, which is not observed in practice, and there was some criticism of the completeness of the chosen model. A. Stein (Germany), in attempting to determine the applicability of the reflexion method to mining problems in Siegerland, had calculated the energies to be expected in longitudinal and transverse waves reflected from siderite veins of various thicknesses. In a more purely theoretical approach to a similar problem, J. Baumgarte, H. Menzel and O. Rosenbach (Germany) dealt with the reflexion of longitudinal waves at a thin layer lying between media of differing velocities. The frequency spectrum and the energy/time relationships were discussed both for sinusoidal plane waves and for an incident pulse of arbitrarily chosen form. Although necessarily somewhat limited by the initial assumptions, this was felt to be a very promising step in the investigation of changes of seismic pulse wave-forms. In a further paper on reflexion surveying, W. Brauch (Germany) considered the travel-time curves with particular reference to the possibility of determining velocity distribution.

Three papers were concerned with the more practical aspects of seismic surveying. W. M. Jones and A. T. Dennison (Great Britain) described a portable geophone, designed for long-distance refraction surveys, which has a natural frequency of 2 c./s.; while there is some doubt whether this low frequency is required, experimental evidence on the subject is indecisive. The discussion on a protractor, designed by J. Schoeffler and E. Diemer (Germany) to facilitate the computation of refraction results, showed that many computers devise such instruments for the solution of their most frequent problems; apart from those described at the meeting, instruments of similar type though differing in detail have been described elsewhere[2]. For several years, multiple geophone groupings have been used in reflexion surveying to minimize the background noise due to the shot, and H. Richard and M. Rimbaut (France) gave the results of a quantitative field study of the improvement obtained with various linear arrays; this was found to depend, approximately, on the square root of the number of geophones.

A. M. Selem (Italy) gave a comprehensive description of the instrumental and interpretative techniques required for a reflexion survey in a coastal region of Southern Abruzzi, an area characterized by a heavily eroded topography. The use of special vehicles and field techniques has enabled the survey to be mainly truck-borne in spite of the steep gradients encountered. Variations in the near-surface layers and the rapid changes of surface elevation required a detailed investigation of the requisite corrections; although the results have not yet been checked by drilling, it is thought that the techniques applied have been very successful. At the present stage of geophysical prospecting, it is somewhat unusual to hear a new method proposed. In this case, M. Matschinski (France) suggested that measurements of the seismic ground unrest could yield information on the underlying geological structure. Assuming that the seismic background is random in nature, he has applied statistical methods to show that measurements of shear strain and of the particle velocity at the surface are related to the depth and character of the geological formations. While certain instrumental and field problems can be envisaged in the practical application of such a method, it remains an interesting suggestion for the practical use of what are otherwise, like telluric currents in electrical prospecting, merely unwanted background noise.

In the gravity section, three authors were concerned with improved techniques of interpretation. G. C. Colley (Great Britain) discussed the variations in elevation correction factor required to correct readings to the datum level, with special reference to its variation across geological boundaries and structures. Formulæ were given for the case of dipping beds together with a general discussion of the anomalous effects which may result over anticlines and near outcrops, although it was agreed that application of the results would require some prior knowledge of the general geological picture. F. Sumi (Yugoslavia) was concerned primarily with a rather different application, the determination of the depth of an ore-body when its shape may be assumed. K. Jung (Germany) has derived a formula, suitable for numerical computations, for the topographical correction of gravity measurements; this is analogous

to the earlier formula, derived by Schwedyar, for the correction of torsion balance readings.

W. Domzalski (Great Britain) reported a series of gravity measurements made in underground workings, readings being obtained also at points on the surface vertically above those below ground-level. By averaging the rock density values measured in the laboratory, he has obtained good agreement with those calculated from the gravity measurements using the standard value for the mean earth density. A more academic note was struck by S. K. Runcorn (Great Britain), who discussed the recent investigations in Great Britain of the direction of magnetization of rocks, with special reference to sedimentary rocks. Their relevance to theories of continental movements was described, and he emphasized the importance of further measurements to give positive evidence on polar drift and on the relative movements of land masses.

The growing use of geophysical methods in mining operations was typified by a description of a gravity survey in east Carmarthenshire by J. T. Whetton, J. O. Myers and I. J. Watson (Great Britain). This detailed survey around a new colliery site, in an area of complex geological structure, has indicated the presence of various faults as well as anticlinal and synclinal structures. These results should help in the planning of the mine-workings, and it will be interesting to see how closely the present geophysical interpretation agrees with the true geological picture. In a second report on a survey in northern Italy, C. Monnet (Italy) dealt with the extended application of the vertical gravity-gradient method. This has been used with excellent results over the areas of interest, and its use as a quantitative interpretation tool in other similar areas was recommended.

An interesting example of international co-operation was afforded by maps, presented by J. W. de Bruyn (Holland), showing the Bouguer and isostatic isogals over most of Europe and North Africa. These maps are on a 1 : 5,000,000 scale with 5- and 25-milligal intervals, and the Bouguer map clearly illustrates the principle of isostasy. The isostatic isogals, based on the Airy–Heiskanen system, show predominantly positive anomalies, and the features of this map were discussed in some detail. A later edition of these maps will be prepared to include a considerable amount of data received recently, and any further information which may become available will be most welcome. H. Closs (Germany) has prepared, in a similar way, a map showing the magnetic Z-anomalies over Europe. He hoped to make further progress with this, although there were difficulties in combining the results of different field surveys owing to the lack of a common standard of measurement; in the discussion, some doubts were cast on the practical value of such a map. An analogous seismic-velocity map was suggested; but this would clearly require agreement on the aim of such a map and the choice of one of the various possible types of information to be shown.

A paper by V. Baranov (France) provided three charts to help in the interpretation of magnetic surveys. Plotting the observed results and visual fitting to the normalized values on the charts give a rapid interpretation of the observed anomaly. As an example of the use of the charts, he described a mining survey in the Pyrenees where one ore-body, and possibly a second, had been successfully located. The various geophysical well-logging techniques are in widespread use, and J. L. Mathieu and C. Rosoff (France) gave a general account of the methods currently employed, though omitting the continuous velocity logger now available in America, but not as yet in Europe. They described how the original electrical methods, though successful in soft formations, had proved unsatisfactory in hard sandstones and limestones, and they showed how the methods developed since the Second World War had considerably improved the value of well logging in such hard formations. For surface electrical resistivity measurements, O. Koefoed (Holland) proposed a modified method of calculating standard interpretation curves and gave a set of such curves for a three-layer problem. He critically reviewed Hummel's method of interpretation and suggested an amendment to extend its useful range.

Finally, in a paper particularly appropriate to a meeting at The Hague, A. Volker and E. O. Houtsma (Holland) described resistivity measurements made in and near the Zuider Zee to determine the salinity of the subsoil. For the measurements in open water, a special cable had been used which provided nine different electrode combinations for each position on the sea-bed, with a consequent increase in the speed of working. The results are of importance both for agriculture and for the provision of water supplies, a further example of the widespread applications of geophysical surveys. A. T. Dennison

[1] Germain-Jones, D. T., *Geophys. Prospecting*, **2**, 177 (1954).
[2] Vajk, R., *Geophys.*, **19**, 237 (1954).

THEORY OF PLASTICITY

The James Clayton Lecture for 1955 of the Institution of Mechanical Engineers was given by Dr. William Prager, who chose as his subject "The Theory of Plasticity: a Survey of Recent Achievements", and Dr. Prager gives an account, both authoritative and entertaining, of the present position of the plastic theory. After a brief historical review, he states carefully the reasons for adopting simplified mathematical models, and emphasizes that the solutions derived therefrom can only be approximations to the physical truth. He then illustrates the stress–strain relations corresponding to the various simplified theories by reference to the displacements of cleverly devised kinematic models. These models are certainly most helpful as means of conveying a clear conception of the discontinuous stress–strain relations characteristic of the plastic state. Dr. Prager uses them for showing the difference between stress–strain theories based on total and incremental strain, a discussion which reveals clearly the conceptual superiority of the incremental laws.

The application of general plastic theorems in the calculation of ultimate load-carrying capacities in the fields of structural and mechanical engineering is then discussed. Methods of obtaining lower and upper bounds on collapse loads are introduced by reference to a simple structural example, in which plasticity takes the form of deforming hinges in a member subjected to a transverse load. The extension of these methods to continuous bodies, with application to mechanical engineering problems, is then described, and a number of illustrations are given. It is found that, while it is comparatively easy to obtain upper bounds in plane and three-dimensional problems, lower bounds are much more difficult to

realize. Recent advances in the derivation of exact values for critical loads are discussed.

The application of plasticity theory to steady-flow problems in which large plastic deformations occur, although stress and velocity fields do not change with time, is illustrated by reference to the plane problem of sheet extrusion. Another class of problem involving large plastic deformations arises when the shape of the plastically deforming part of a body remains constant, while the size increases as more and more of the originally rigid material becomes plastic. The lecture ends with a short section dealing with dynamic problems, and quotes as an example the case of a beam subjected to a transverse uniformly distributed blast load. The energy given to the beam and stored momentarily as kinetic energy is dissipated in deformation at plastic hinges, which may move progressively along the beam, thus producing plastic deformation over considerable lengths.

Dr. Prager's lecture certainly reveals a remarkable advance in the development of the theory of plasticity in recent years. The large part played by mathematical intuition in the derivation of many of the solutions is evident, and the many cases in which this intuition is successful in achieving solutions to practical problems represent the most stimulating feature of the theory of plasticity for the engineer. As progress continues, the place of intuition declines and systematic analysis takes its place. This survey has been made at a time when the second stage is well under way in many branches of the theory—a period full of danger as well as promise. The danger is that mathematical models found successful for certain problems may be applied indiscriminately under conditions where they become quite inadequate. This is revealed most clearly at the end of the lecture in the section dealing with dynamic loading, where a factor of over-riding importance, namely, the effect of rate of strain on the stresses producing the deformation, is scarcely mentioned. The lecture is concerned with the theory of plasticity, of which it is a most outstanding and opportune summary. It is for the engineer who applies the theories to satisfy himself that the mathematical model on which the theory is based is appropriate to his problem, either by fundamental investigations or by carrying out suitable tests under practical conditions. M. R. Horne

CARNEGIE INSTITUTION OF WASHINGTON

REPORT FOR 1953–54

THE report of the president of the Carnegie Institution of Washington, Dr. Vannevar Bush, for the year ended June 30, 1954*, explains in some detail the features of the new retirement plan which came into operation on July 1, 1954. He discusses the principles on which it is based, notably the importance of reaching understanding with those affected at the outset, and securing individual assent in advance to whatever changes or modifications are seen from time to time to be desirable to serve the best interests of the group concerned and provide a balanced provision against the risks which savings inevitably face. Of the research activities of the Institution, Dr. Bush notes that fully half the observing time of the 60-in., 100-in. and 200-in. telescopes at the Mount Wilson and Palomar Observatories continues to be devoted to spectroscopic and photometric studies of individual stars. Preliminary results of the spectroscopic investigations of globular cluster stars during the past two years indicate a lower excitation temperature for a given spectral class, and a substantially lower abundance of the metals than is found in population I, while photometric studies have revealed large differences between the two populations in the relation between total luminosity and surface temperature. In co-operation with the National Bureau of Standards, the United States Naval Observatory and the California Institute of Technology, the Institution is examining whether electronic image-conversion techniques offer a means of extending the range of large telescopes or increasing the utility of those of moderate size.

The Department of Terrestrial Magnetism reports considerable progress in our understanding of the structure of the atomic nuclei, based on the observation that most nuclei from fluorine to uranium can be made to radiate characteristic gamma-ray lines when bombarded by relatively low-speed helium ions from an electrostatic generator. About a hundred and fifty energy-states have been detected in some seventy nuclei examined at the Department by this 'Coulomb excitation' process. Experimental observations at the Geophysical Laboratory are gradually providing a quantitative basis for understanding the various assemblages of minerals found in the metamorphic rocks and have led to the synthesis of many minerals found in such rocks, including a series of micas and garnets, the ranges of stability of which as functions of temperature and pressure have been determined. Other studies have demonstrated that the recurrence of proteins in hard parts of recent creatures is widespread and that under favourable conditions fossils may contain amino-acids such as alanine, glycine, valine, leucine, aspartic acid and glutamic acid after 360 million years.

In the Department of Plant Biology, spectral changes of unidentified substances have been found in illuminated *Chlorella* suspensions. The work on grass this year has shown that environment may greatly influence the percentage of aberrant or 'off-type' plants that may appear in a stabilized, asexually reproduced strain. Under conditions of intense competition in unfavourable environments, the percentage of sexually produced variants may increase greatly in relation to the normally predominant asexual plants. The absolute absorption spectra of purified chlorophylls *c* and *d* and of bacteriochlorophyll have been determined, thus providing a means of determining these pigments in plants which use them for photosynthesis. Studies of forests on both sides of the Pacific suggest that the coast redwood was not a tree of the coast during much of its hundred-million-year history, but lived at higher elevations in the interior of North America.

Experiments on *Salmonella typhimurium* in the Department of Genetics indicate that a gene locus occupies a longitudinal section of the chromosome, and that changes occurring in different parts of the locus give rise to different new forms of the gene, that is, alleles. Recent work on the genetic mechanism of bacterial viruses indicates that viral nucleic acid controls viral inheritance, while studies of cell chemistry have focused attention on the importance of the nucleoprotein complex in vital cellular activi-

* Carnegie Institution of Washington. Report of the President for the Year ending June 30, 1954. Pp. 15. (Washington, D.C.: Carnegie Institution of Washington, 1954.)

ties. Notable progress has been made in the Department of Embryology in the analysis of the control of sex differentiation in the embryo by the action of sex-gland hormones; and a long-term study of the blood flow through the placenta, first in monkeys bred for the purpose, and afterwards on human placentas, points to physiological factors—that is to say, differences in blood pressure between the maternal arterial and venous blood and the blood within the placenta—as the chief directive agency of the maternal placental circulation, assisted by anatomical features of placental structure. Experiments on pregnant rhesus monkeys suggest that sugar metabolism in the primate placenta is not like that in sheep, at least with respect to glucose and fructose. The Department of Archæology continued its researches dealing with the preconquest history of Yucatan.

RELATIONSHIP OF SCIENCE AND RELIGION

IN his Rede Lecture for 1954 on "Science and Religion: a Changing Relationship", which has now been published*, Prof. C. A. Coulson, pointing out that Nature (by which he means the totality of our environment) and man are central both to science and religion, maintains that the division of our experiences into those labelled scientific and those labelled religious is wholly unsatisfactory and false to the true character both of science and religion. Science claims to give an account of all our environment, and he believes that the limits of science are only those which are presented by the words: if a question about Nature can be posed in scientific terms, then ultimately it will be susceptible of a scientific answer. In remarking that every scientific law is a new imaginative conception, Prof. Coulson suggests that, like the artist, the poet and the saint, the scientist is making sense out of that part of his experience which appears most amenable to his own selective understanding; he is looking for a pattern within them which will satisfy him as reasonable and consistent. Science is one kind of pattern, art is another.

Our loss of immediacy in our relation to Nature has, Prof. Coulson thinks, increased rather than diminished the contrast between conventional science and religion. Among the scientists of to-day there are respect and excitement, sometimes astonishment, but all too seldom reverence; and if we could recognize that man's total response to Nature must include not merely the making of a pattern that may be called true but also the recognition that God is mediated to him both in the experience and in the pattern, science would be recognized as one of the languages in which God is revealed, and the work of scientists would be seen as part of God's work. The sense of immediacy, which has largely been lost in modern scientific study, would be rediscovered. Our approach to the study of man is also changing, and here Prof. Coulson thinks science can help religion by forcing us to see and understand the sacramental value of Nature and the wholeness and unity of things. Science is also a powerful and insistent reminder of the worth of reason at a time when men's faith in the virtues of reason is wavering. A faith in rationality is central to the Christian tradition at its finest. Science is also affecting our view of the role of men within the whole pattern of Nature. Men and Nature are inextricably mixed, and Prof. Coulson believes that science has something to say about the very structure of human fulfilment, for which Christians have greater reasons for being grateful than they sometimes admit. There is a liberating quality about scientific thinking to-day, and yet a humility, which seems to him to augur well for a future complementary relation between science and religion.

In its methods of working, in its dependence upon the assumption of a spiritual wholeness about life, in its insistence upon the richness and variety of experience, and the inter-relatedness of all things within the role of a person, continued Prof. Coulson, the changing pattern of science has come back to something more like harmony with the Christian faith. In that new harmony there are new notes which would never have been sounded but for the patience, the integrity and the creative imagination of men of science. Lastly, all scientific beliefs are experimental in character, and the concepts of science acquire their validity only in experience. This is also true of the Christian faith, and it is one more debt which religion owes to science.

* Science and Religion: a Changing Relationship. (Rede Lecture for 1954.) Pp. 36. By Prof. C. A. Coulson. (Cambridge: At the University Press, 1955.) 2s. 6d. net.

BURSTS OF RADIO EMISSION

R. D. DAVIES has published a paper entitled "An Analysis of Bursts of Solar Radio Emission and their Association with Solar and Terrestrial Phenomena" (*Mon. Not. Roy. Astro. Soc.*, **114**, 1; 1954), which presents a detailed analysis of bursts of radio emission recorded at the Radiophysics Laboratory, Sydney, during January 1950–June 1951. This analysis includes a detailed study of the correlation of bursts with flares, sunspots, ionospheric fade-outs and magnetic crochets. While attempts to draw physical conclusions from the analysis have not been made in most cases, nevertheless certain results of immediate interest are briefly discussed. The radio data were obtained mostly from records at 200, 600, 1,200, 3,000 and 9,400 Mc./s., and in the latter part of the analysis these were extended to 62 and 98 Mc./s. All these came from the records taken at the Radiophysics Laboratory, Sydney, except the first, which came from records from the Commonwealth Observatory, Mt. Stromlo.

The analysis—in two parts—includes a number of histograms, and shows that many of the properties of bursts change with frequency (a burst is defined as "any clear-cut solar radio emission rising above the daily level"). A characteristic of bursts is their 'jaggedness', that is, short-duration rises and falls in intensity, and the degree of jaggedness decreases with increasing frequency. Tables, figures and histograms show that there are many interesting relations between the number of bursts and their frequencies, and also between bursts and sunspots, flares, fade-outs and crochets. As the frequency of bursts rises from 600 to 9,400 Mc./s., their average number per hour diminishes from 0·10 to 0·04, and the average interval between the bursts increases from 10 to 26 hr. A number of figures shows the distribution of the lifetime of the bursts at the different frequencies, the distribution of their decay times, the distribution of their intensities, etc.

The second part of the analysis deals with the relation between radio data and sunspot data, and to do this an estimate was made of the average number of bursts per hour for each month; Fig. 7 gives a comparison of the three-month running means (number of bursts per hour) with the monthly average sunspot areas and numbers for the period referred to earlier. From this figure the following conclusions are drawn: (1) time plots of the burst index are similar at different frequencies; (2) there is a good correlation between the burst index and the sunspot area and number. Additional important results are the coincidences between flares and excess radio noise; at least 99 per cent of all flares are accompanied by excess radio emission in some part of the frequency-range, but it is admitted that this high correlation may be due to chance coincidences. So many other matters are dealt with that it is impossible to consider them all here. One further point, however, may be mentioned, namely, magnetic storms and world-wide crochets, briefly referred to in the appendix. On four occasions, listed in Table 6, the sudden commencement of a magnetic storm was preceded by a burst but not a flare, the time delay between burst and commencement of the magnetic storm varying between 20h. 58m. and 29h. 13m.; Table 7 lists eleven world-wide crochets, not accompanied by a reported flare, associated with bursts, between February and November 1950. These phenomena, it is stated, appear to be genuine and may be supposed to have a flare-like origin, judging from their association with bursts.

EARTHQUAKES DURING OCTOBER 1954—JANUARY 1955

DURING the last three months of 1954 there were in the world twenty-four earthquakes having instrumental magnitude 6 or greater. The greatest two had magnitude 7 and occurred on October 21 in the South Indian Ocean, and on December 16 near Fallon, Nevada. The latter caused moderate property damage. The earthquake of deepest focus during the period had a focal depth of 650 km. and occurred on November 25 in the Fiji Islands region. There were two minor British earthquakes. On the afternoon of October 23 South Elmsall (Yorkshire) was affected by a severe tremor which shook furniture and crockery. The shock was also felt at Hemsworth and Pontefract. On November 15 at 6.25 a.m. Winster, in Derbyshire, was shaken by an earth tremor felt with Modified Mercalli intensity 4, which rattled crockery, pictures and furniture. The shock was also felt at Birchover and Elton. Both these earthquakes were accompanied by low rumbling sounds. Previous tremors at Winster occurred in February 1952, and before that in 1903–4.

In other parts of Europe, earth tremors were reported to have occurred in October near Trieste, near Innsbruck and in Spain. On November 16 an earth tremor occurred forty miles south of Rome, and on November 23 at Grisi, near Palermo, in Sicily. The following month nearly all the houses on Salina Island (about fifty miles from Messina) were damaged in an earthquake swarm which began on December 23. Possibly associated with this, there was a lava flow accompanied by steam from the crater of Stromboli, while from Etna there issued a column of smoke mixed with ash. Shocks and volcanic activity ceased by January 3. On December 23 an earthquake occurred in western Peloponnesus, injuring nineteen people and causing the collapse of several houses.

Elsewhere, on December 4 an earthquake with instrumental magnitude 6¼ and depth of focus 60 km. occurred near Trinidad. One person was killed, several injured, and there was extensive property damage, including damage to Government House and both the Anglican and Roman Catholic Cathedrals. On December 21 an earthquake of instrumental magnitude 6½ occurred in Humboldt County, California, injuring several persons and causing extensive property damage.

During January of this year there were reports of eight earthquakes with magnitude 6 or greater. The greatest occurred on January 13 in the Fox Islands (Aleutian Islands). It was felt at Unalaska and had logarithmic magnitude 6·9. The shock with the greatest depth of focus occurred on January 22 in the Fiji Islands, its depth of focus being 650 km. The only shock reported as having caused property damage occurred on January 25 on the Tennessee–Arkansas–Missouri borders. The damage was of a minor character.

FORMATION AND CHARACTERISTICS OF LATERITE

THE dark-red, hard, barren, slag-like, acre-wide sheets of laterite commonly seen in the tropics have led many to conclude that this is the final wretched residue of soil-forming processes and represents the death of the soil. The origin of these impressive formations has long been disputed. Weathering has apparently been associated with removal of silica and bases; but that seems to be the case also with two other materials: Buchanan's laterite, a soft, vesicular, red earth which hardens on exposure and has long been used as building stones; and the deep, very friable, porous, dark-red, well-drained soils of forested slopes. Each of these materials consists largely of sesquioxides, and it has seemed remarkable that they differ so strikingly in their physical properties.

Dr. J. D'Hoore, director of the Service Pédologique Interafrican and a distinguished member of the staff of the Institut National pour l'Étude Agronomique du Congo Belge, has thrown a welcome light on this problem by distinguishing 'absolute' and 'relative' accumulation of sesquioxides in soil*. He remarks that the concentration of a salt solution can be increased by adding salt (an absolute accumulation) or by removing solvent (a relative accumulation). Similarly, a low-lying area can receive an inflow of ferruginous solution, an absolute accumulation, and a high-lying area can suffer loss of silica and bases and thereby exhibit a relative accumulation of sesquioxides.

In the case of the low-lying area attention is given to the physical and chemical nature of the substrate (for example, mixed colluvial material) that receives the absolute accumulation of sesquioxides, and in the case of the upland area attention is given to the

* Publications de l'Institut National pour l'Étude Agronomique du Congo Belge. Série Scientifique No. 62: l'Accumulation des sesquioxides libres dans les sols tropicaux. Par Dr. J. D'Hoore. Pp. 132. (Brussels: Institut National pour l'Étude Agronomique du Congo Belge, 1954.) 80 Belg. francs.

physical and chemical nature of the parent rock which undergoes a relative accumulation, this being another name for the process that leads to the formation of a sedentary soil of the Red Earth class.

Fripiat and Gastuche observed that an iron oxide sol if flocculated will form hard, coherent flakes; but if the flocculation is carried out in presence of clay under certain conditions, the iron is adsorbed on to the clay particles, and these remain loose and incoherent until their capacity for adsorption is exceeded. D'Hoore considers that in Nature also a similar process accounts for the more ready formation of hard crusts and hard concretions in a medium that is coarse and low in clay content.

In agreement with many other authorities, D'Hoore observes that a low-lying zone of absolute accumulation may be buried under new deposits or, if drainage improves and a cycle of erosion intervenes, may end up as the resistant capping of a flat-topped hill. These lateritic crusts (*cuirasses*) are liable to mechanical breakdown and to chemical dissolution, the latter being mainly due to formation of complexes with organic materials derived from growing plants. If the underlying material is well supplied with plant nutrients, fertile soils may result from the decomposition products of the lateritic crusts.

In considering the classification of these sesquioxidic accumulations, D'Hoore considers first whether accumulation is in progress, whether it has stopped, or whether breakdown has begun. Within these major categories it is possible to recognize four modes of accumulation: *A*, absolute; *Ar*, the same with some relative enrichment; *R*, relative; and *Ra*, the same with some absolute enrichment. For an example of *Ar*, there is the low-lying accumulation on a substrate which is itself liable to removal of silica and bases. For an example of *Ra* we have the deep Red Earth in which plant roots bring into solution and mobilize a part of the abundant sesquioxides that are afterwards immobilized, forming a cement for particles that were previously loose. Further classification of the sesquioxidic accumulation proceeds on a logical plan, and illuminating accounts are given by Dr. D'Hoore of the visible characters of the various products and of the laboratory data, such as chemical analysis, differential thermal analysis and examination under the electron microscope, which can supplement field observation of morphology.

The publication is illustrated with well-chosen photographs and diagrams. It marks a memorable advance in our knowledge of some of the soil-forming processes which profoundly influence agricultural development in the tropics. In this field it will add to the already high prestige of the scientific work sponsored by the Institut National pour l'Étude Agronomique du Congo Belge.

ORIGIN OF THE VIRUS-PRODUCING CHROMATIC MASS OR NET OF THE INSECT NUCLEAR POLYHEDROSES

By N. XEROS

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MANY authors, including Marzocchi[1] and Glaser[2], have maintained that the pathological intranuclear chromatic mass or network of the infected lepidopteran cell is a stage in the further development of a fused aggregation of nucleoli. This view, however, is certainly erroneous. Paillot[3] and Heidenreich[4] considered that the chromatic mass in a number of Lepidoptera is formed primarily by the fusion of chromatin granules of the pathological nucleus. (Paillot's and Heidenreich's further claim regarding the presence of supposed nucleolar remnants and their deposition on the chromatic masses is mistaken.) Bird[5], in the case of a nuclear polyhedrosis in sawflies, and Xeros[6], in a number of Lepidoptera, also ascribed its origin to the association of chromatin granules. Certainly there are appearances which suggest this interpretation. However, a more detailed examination of this aspect of the cytology of several nuclear polyhedroses failed to support it. It appears that the chromatic mass does not arise from any of the recognizable pre-formed bodies of the nucleus.

The nuclear polyhedroses investigated were those of the fat body and hypodermis of the Lepidoptera *Abraxas grossulariata*, *Lymantria dispar*, *Bombyx mori*, *Pyrameis atalanta* and *Panaxia dominula*; of the midgut of *A. grossulariata* and *B. mori*; and of the midgut of a sawfly, *Neodiprion sertifer*. In this work, Carnoy-fixed material was examined both with and without acid hydrolysis and ribonuclease extraction. Some deoxyribonuclease extraction was also done. The most useful stains used were Giemsa, Schiff's reagent, toluidine blue and bromophenol blue. Some material fixed in formalin and osmic acid was also examined, as well as some live material. All the consecutive sections of many given nuclei at different stages of development of the disease were studied, and care was taken to ensure that the possibility of confusing nucleoli with the earliest stages of the chromatic net in material extracted with hydrochloric acid was avoided.

At about half-way through the infection cycle of the hypertrophied infected cell, there is a tendency for aggregates of nucleoli and chromatin granules to form. Some nucleoli fuse, others elongate, etc. About this time the chromatin granules, apart from those retreating to the nuclear membrane, either become closely associated with the surfaces of the nucleoli or remain loosely associated with the nucleolar clumps. At the same time the true chromatic masses make their appearance for the first time in the form of small patches, sheets or branching lobes of protein material which arise in between and peripherally to the nucleolar aggregates. The topographical relations at this stage, and for a long time after, may perhaps best be described as those of interdigitation or interlacement, the chromatic mass or masses in a nucleus interdigitating with the nucleolar masses.

The chromatic mass(es) as it grows, the nucleus itself meanwhile expanding, develops progressively

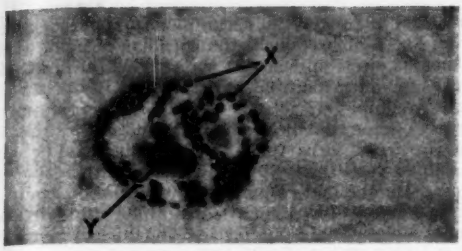

Fig. 1. Fat body cell of *Abrazas glossulariata*. *X*, discrete chromosome-nucleoli. *Y*, moderately developed chromatic net the pores of which at this stage are just resolvable by the light microscope. Photo retouched. × 1,750

into one or several well-defined bodies tending to occupy one or other end, side or centre of the nucleus. More or less of a definite ring-zone appears, depending partly on the relative size of the nucleus and its chromatic mass(es), and partly on the degree to which the nucleolar material lies close to the nuclear membrane away from the chromatic mass or continues to intertwine with or dissect the latter. Heidenreich is mistaken in believing that the chromatic mass shrinks and, therefore, becomes denser and more Feulgen-positive, in the course of the disease. There are a tremendous growth and increase in amount and concentration of both the protein and deoxyribonucleic acid of the masses.

There is no simple coagulation or fusion of chromatin granules (as stated by Hughes[7]) to give a chromatic mass as strongly Feulgen-positive as the chromatin granules themselves, or staining with the same intensity or colour with toluidine blue or Giemsa. When first formed, the chromatic mass is almost completely Feulgen-negative and achromatic, and with toluidine blue stains a pale-greenish wash. Were its origin from the chromatin granules, it could only be from dispersing material of 'disintegrating' granules, which would lose their strongly Feulgen-positive and chromatic nature. In many nuclei the cytological picture partly suggests this; that is to say, at the time the chromatic mass first appears, the chromatin granules may be very small, irregular and dispersed. But the evidence goes no further than that. In my material the chromatin granules of the fat cells, for example of *A. grossulariata* and *L. dispar*, were large, definite and discrete chromosome-nucleoli (Fig. 1); and in *A. grossulariata* in particular, but also in the majority of *L. dispar* nuclei, they remained so throughout the formation of the chromatic mass. In *A. grossulariata* they remained so right up to the maximum growth and enrichment of the chromatin net with deoxyribonucleic acid. In *L. dispar* they tended to unravel as the chromatic net grew. In *Pyrameis atalanta* the numerous chromatin granules, though definite and discrete, were smaller than in *L. dispar* and *A. grossulariata*. Apart from those on the nuclear membrane, they were intimately associated with the very elongated nucleoli. Throughout the formation and most of the growth of the chromatic net, the granules did not tend to unravel. In none of the material examined was any evidence found that the chromatic mass had been formed from the chromatin, whether this existed as unmistakable chromosome-nucleoli, or was unravelled to various extents. Indeed, as already noted, in the bulk of the nuclei of certain tissues the chromatin granules remained as chromosome-nucleoli throughout the formation and most of the growth of the chromatic masses. The cytology of the nuclear polyhedroses of the gut and of the other tissues, in the Lepidoptera and in the sawfly, were found to be essentially the same. From these observations it is concluded that the chromatic masses of these nuclear diseases do not arise by fusion of chromatin granules but are produced *de novo*.

In Carnoy-fixed material of the peculiar nuclear polyhedrosis of the blood cells of *Tipula paludosa*, I have found[8] that the chromosomes of the telophase cluster elongate and become applied to the nuclear membrane. A proteinaceous inclusion body, almost completely Feulgen-negative, forms in the nuclear sap. It enlarges and becomes deeply Feulgen-positive. At, or just prior to, polyhedron formation the chromosomes become detached from the nuclear membrane. All the evidence so far obtained points strongly to the central body as the site of formation of virus rods. In this disease, as in those of the Lepidoptera and sawflies, the chromatin may play an important, even 'secretory', part in the formation of the virus-producing inclusion bodies; but the latter do not seem to arise directly from the chromatin material.

The material of the chromatic mass, almost from its very formation, is recognizable as an exceedingly

Fig. 2. Portion of fat-body cell of *Lymantria dispar* at early stage of polyhedron formation. *V*, cytoplasmic granules. *W*, nuclear double membrane. *X*, vesicles attached to nuclear membrane. *Y*, developing polyhedron with occluded virus rods in capsules. *Z*, incompletely formed capsule membranes surrounding virus rods. × 50,000
Electron micrograph taken by Mr. R. Horne, Cavendish Laboratory, Cambridge

fine three-dimensional network and retains this basic structure throughout its further enrichment with protein and deoxyribonucleic acid, though the network is obscured when it is most heavily laden with virus. No ribonucleic acid has been detected in it at any stage of its development. During the development of the chromatic mass the nucleoli tend to be vacuolated. In the course of the disease the ribonucleic acid and protein of the cytoplasm increase markedly.

The chromatic net retains its basic structure until most of the deoxyribose nucleoprotein virus formed on it has been set free into the ring-zone; one cord of it after another may then dissolve and the mass expand and take on the appearance of a coarse network during the period of polyhedron formation. In fine sections of *L. dispar* fat body, it has been found that no virus rods are present on the fine chromatic net when it is first formed. The virus rods form in the cords and are later freed into the ring-zone. Virus may aggregate and polyhedra also form in large pores of the early net. In *L. dispar* the density of freed virus rods is far higher in some of these pores than in the ring-zone. Due to this, the number of virus rods which associate together to form a single bundle is much greater in the former position. It has also been found in *L. dispar* that the inner capsule membranes form around the freed individual rods or aggregates of them, surrounding one end first and then gradually completely enclosing them (Fig. 2). Synchronously the capsular protein, which is not as electron-dense as the polyhedral protein in the osmic-fixed material, is deposited within the more or less completely formed part of the capsule membrane. Somewhat prior to the formation of capsules on the freed virus rods, large numbers of peculiar θ-shaped vesicles 30–70 mμ in size appear in the ring zone. By the end of polyhedron formation many of these seem to have been transformed into 'ribbons' about 500 mμ × 12 mμ in size. The nuclear boundary of the fat cell is a double membrane.

I am indebted to Dr. K. M. Smith for the diseased sawfly larvæ and many of the other viruses, to Dr. R. Markham for the samples of ribo- and deoxyribonucleases used in this work, and to Prof. G. Causey and Dr. H. Hoffman for making available technical facilities at the Anatomy Department of the Royal College of Surgeons for cutting the sections for the electron microscope. [Jan. 3

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CONDUCTIVITY INDUCED BY X-RAYS IN POLYETHYLENE TEREPHTHALATE: A POSSIBLE INSULATOR FOR RADIOLOGICAL APPARATUS

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MEASUREMENTS of the conductivity induced by X-rays in 'Melinex' (polyethylene terephthalate sheet) have been made, using the d.c. amplifier technique previously described[1,2]. The specimens consisted of sheets of 'Melinex' film 0·03 mm. in thickness placed in a chamber that could be evacuated. The magnitudes of the static and induced conductivities have been measured in addition to the dependence of induced conductivity upon temperature and dose-rate, and the shape of the decay curve after irradiation.

The induced currents are smaller than in any of the other materials we have investigated; the equilibrium induced current varies with dose-rate in a way that follows more nearly a linear than a square root law; and when irradiation ceases, the current falls within a few seconds to a small fraction of the equilibrium value. These three characteristics lead us to distinguish 'Melinex' on one hand from the class of insulating materials such as 'Perspex' (plasticized) and some types of amber[1], which follow almost exactly a linear law, and on the other from the class of materials described recently[3] having $\Delta = 0{\cdot}6$ (see equation (1) below). The second class includes polystyrene, polytetrafluoroethylene, unplasticized 'Perspex', and polyethylene. The division cannot be regarded as rigid, and both polyethylene and 'Melinex' tend to 'bridge' the gap, with 'Melinex' closer to the first-mentioned class and polyethylene closer to the second.

Dependence on dose-rate. In the relationship between equilibrium induced current i_x and dose-rate, R,

$$i_x \propto R^{\Delta} \qquad (1)$$

we find $\Delta = 0{\cdot}83 \pm 0{\cdot}05$ for 'Melinex' film, over the range $R = 6$–64 r./min., and between 20° C. and 100° C. This value of Δ is close to that of polyethylene[3], for which $\Delta = 0{\cdot}80 \pm 0{\cdot}05$. An exponential distribution of trapping-levels in energy below the conduction band is therefore to be expected, the number of traps N_W between W and $W + \mathrm{d}W$ electron volts below the conduction band being given by

$$N_W = A \exp(-\alpha W) \qquad (2)$$

where A is a constant. The theory of photoconductivity from which we have previously drawn analogies[4] gives

$$\alpha = 1/kT_1 \qquad (3)$$

where k is Boltzmann's constant and T_1 is an arbitrary temperature, characteristic of the material. In addition,

$$\Delta = T_1/(T + T_1) \qquad (4)$$

so that α can be determined from the observed value of Δ.

For 'Melinex' at 50° C., it is found that $T_1 =$ 1,700° K. and $\alpha = 6{\cdot}8$. The number of traps at a given depth below the conduction band therefore falls

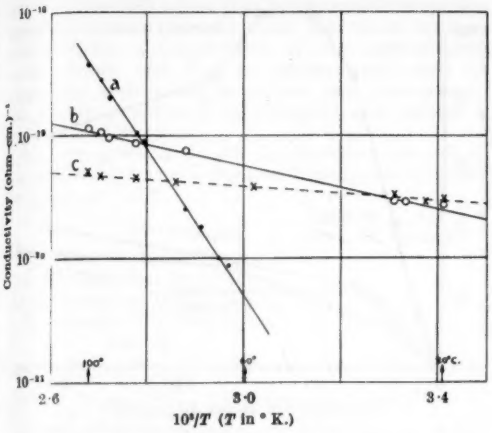

Fig. 1

to one-half for each 0·1 eV. increment of depth. The corresponding decrease in the case of polyethylene ($\Delta = 0{\cdot}8$) is to one-third. (In polystyrene ($\Delta = 0{\cdot}6$), the number of traps falls to 7 per cent for each increment of 0·1 eV. (class 2), whereas in a material with $\Delta = 1$ the distribution of traps is constant with depth.)

The variation of Δ with temperature T given by equation (4) is in fact observed for 'Melinex', as in the case of polytetrafluoroethylene and polystyrene[2].

Dependence on temperature. Fig. 1 shows the graphs of log (conductivity) of 'Melinex' plotted against the reciprocal of absolute temperature. The resulting straight lines are of slope proportional to the activation energy W, according to the general formula

$$\sigma = \sigma_0 \exp(-W/kT) \qquad (5)$$

In the case of static conductivity (that is, with no incident radiation; Fig. 1*a*) $W = 1{\cdot}3$ eV. This is a similar activation energy to those found in the other insulating plastics we have studied. For the equilibrium-induced conductivity under X-irradiation (Fig. 1*b*) at $R = 7$ r./min., the slope corresponds to an activation energy $W = 0{\cdot}2$ eV. This is considerably less than the materials of class 2 above ($W = 0{\cdot}5$ eV.), and less than for polyethylene, for which $W = 0{\cdot}35$ eV.

Plasticized 'Perspex' and moulded amber, however, have been found to show even less dependence of i_x upon temperature than 'Melinex', and this is explained not necessarily by a small activation energy, but by a uniform distribution of traps. Using the exponential distribution derived above for 'Melinex', the induced current would be expected to increase by a factor of 3 between 20° and 80° C. The observed increase is in good agreement (Fig. 1*b*).

Effect of removing air. When the specimen was kept under vacuum at 60° C. for several hours prior to irradiation, the dependence of i_x upon temperature became markedly less, an increase of only 1½ being observed between 20° and 80° C. The magnitude of the induced current decreased, but only at the higher temperatures (Fig. 1*c*). This observation is consistent with the removal, as the specimen chamber is evacuated, of some of the shallower traps (< 1 eV.), making the distribution more nearly uniform. These traps are probably due to the presence of adsorbed gas[5]. The same phenomenon occurs to an even greater extent in 'Perspex', but scarcely at all in polyethylene, polystyrene or polytetrafluoroethylene.

Decay of the induced current. As in the other plastics studied, the conductivity persists after switching off the radiation, decaying rapidly at first and then more slowly. In 'Melinex' the rapid decay is to between 1/3 and 1/20 (depending on temperature and dose-rate) and it occupies only a few seconds; in this respect it is similar to polyethylene. The equilibrium conductivity in polyethylene, however, and therefore the current remaining after the initial rapid decay, is much greater (10^3–10^4 times) than in 'Melinex'.

The subsequent decay follows the general hyperbolic relation

$$\frac{1}{i} = \frac{1}{i_x} + Ct \qquad (6)$$

where i is the current at time t after irradiation ceases, and C is characteristic of the material, varying slowly with temperature. This equation is valid between $t \approx 5$ min. and $t \approx 5$ hr.

Plotting reciprocal fraction of current against time gives $C = 20$ min.$^{-1}$ for 'Melinex' at 85° C., so that the time taken for decay from 10 per cent to 1 per cent would be 20×90 min., that is, 30 hr., if equation (6) remained valid. It is found, however, that the decay becomes approximately exponential at longer times, so that 'Melinex' at 85° C. shows virtually complete recovery after about twelve hours. At lower temperatures, this slow decay takes much longer, but is still much more rapid than in polytetrafluoroethylene and polystyrene; and, of course, the currents remaining in 'Melinex' at these long times are extremely small.

Under vacuum, the initial rapid decay is even greater, the fraction i/i_x remaining after 1 min. being reduced by a factor between 2 and 10, depending on temperature and dose-rate. This accords with the deduction above that some of the less deep traps are removed. Thus, under vacuum, 'Melinex' becomes less like polyethylene, and more like the materials of class 1.

Application to radiology. Polyethylene terephthalate appears to be basically suitable as a high-insulation material for use in condensers or radiological instruments which operate in the presence of ionizing radiation. This suitability is due to: (*a*) its high natural insulation; (*b*) its low induced conductivity; and (*c*) the initial rapid decay of the induced current, after irradiation, to very small values. Its performance in all these respects is improved if the insulator is operated under a vacuum, but this condition can, of course, seldom be met in practice.

Polyethylene terephthalate is not yet made in the form of rods or blocks, but the 'Melinex' sheet already available may find applications in condenser construction. Further tests of dielectric strength, mechanical properties, and incidence of flaws would, of course, be required to assess more fully its potential uses as an insulating material.

We thank I.C.I., Ltd. (Plastics Division, Welwyn Garden City), for their co-operation in supplying the samples of 'Melinex' film. [Dec. 22

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LETTERS TO THE EDITORS

The Editors do not hold themselves responsible for opinions expressed by their correspondents. No notice is taken of anonymous communications

Promotion of Incorporation of Amino-acids by Specific Di- and Tri-nucleotides

When disrupted staphylococcal cells are incubated with ^{14}C-labelled amino-acids and a source of energy, the radioactive amino-acids become incorporated into the protein of the preparation. When only one amino-acid is present in the incubation mixture, incorporation appears to take place by a process of exchange occurring between the added ^{14}C-labelled amino-acid (or a metabolite thereof) and corresponding residues in the cell protein. In many cases the incorporation can be largely abolished by removal of nucleic acid from the disrupted cells, and then restored by addition of staphylococcal nucleic acid; but the magnitude of these effects varies with the amino-acid the incorporation of which is being studied[1]. These differing effects could be explained if the incorporation of specific amino-acids were activated by specific portions within the polynucleotide structure, some parts of which were more easily damaged, or replaced, than others.

The incorporation of glycine or aspartic acid can be activated by addition of nucleic acid from staphylococci but not from other cells. Staphylococcal nucleic acid is not inactivated by digestion with ribonuclease, whereas nucleic acids from yeast or liver become active after such digestion. Therefore we have proceeded to fractionate ribonuclease digests of staphylococcal ribonucleic acid, using chromatography and ionophoresis on paper as described by Markham and Smith[2], in an attempt to separate the fractions in the digests which are necessary for activation of the incorporation of certain amino-acids under exchange conditions. Disrupted staphylococcal cells have been prepared and depleted of nucleic acid as previously described[1], and the rates of incorporation of ^{14}C-labelled aspartic acid, etc., determined in the presence and absence of ribonucleic acid or fractions obtained from digests thereof. Active materials have been identified by reference to the data given by Markham and Smith[2], and by estimation of the purine bases or pyrimidine nucleotides liberated by hydrolysis in *N* hydrochloric acid. In the cases so far investigated, of aspartic acid, glutamic acid, glycine and leucine incorporation, it has been possible to replace ribonucleic acid by materials occurring in the di- or tri-nucleotide fractions.

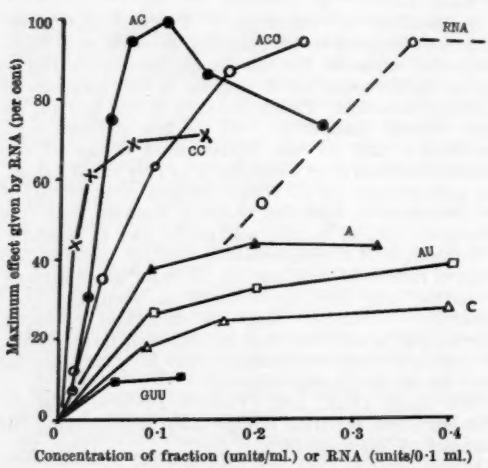

Fig. 1. Replacement of ribonucleic acid by nucleotides for the activation of aspartic acid incorporation in disrupted staphylococci. Incubation mixture contains buffered saline *p*H 6·3, adenosine triphosphate, hexosediphosphate, ^{14}C-labelled aspartic acid, and staphylococcal ribonucleic acid or nucleotides as indicated (*A* = adenylic, *G* = guanylic, *C* = cytidylic, *U* = uridylic acid). 1 unit = amount of material having extinction 1·0 at 260 mμ. Ribonucleic acid concentrations reduced to 1/10

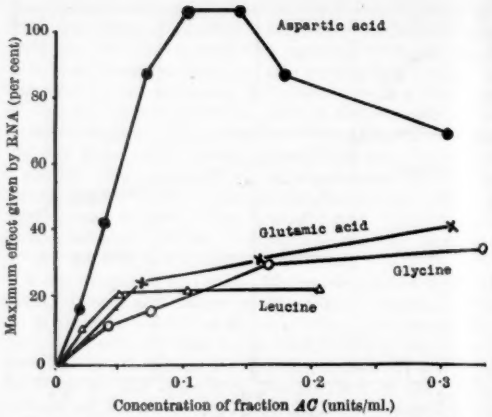

Fig. 2. Action of *AC* (adenine–cytosine dinucleotide) in replacing ribonucleic acid for the activation of incorporation of various amino-acids in disrupted staphylococci

Fig. 1 shows the effect of various nucleotide fractions in activating aspartic acid incorporation; *A*, *G*, *U*, *C* refer to adenylic, guanylic, uridylic and cytidylic acids respectively. The fraction '*AC*', which contains adenine–cytosine dinucleotide, completely replaces ribonucleic acid and, compared on a basis of optical density at 260 mμ, is 110 times as active as the whole ribonucleic acid. Many of the fractions tested showed some activity for aspartic acid incorporation, but, except in the cases of *AC* and *ACC*, the replacement of ribonucleic acid was only partial; thus *C* gave 25 per cent and either *A* or *AU* 50 per cent replacement of the ribonucleic acid effect. Replacement by the fractions reaches a plateau value and decreases again at high concentrations; even in the most effective cases (see *AC* in Fig. 1) complete replacement is obtained over only a short range of concentration. Fig. 2 shows the action of *AC* in replacing ribonucleic acid for activation of the incorporation of other amino-acids; complete replacement is obtained only in the case of aspartic acid of the four amino-acids tested.

Ribonucleic acid can again be replaced by small polynucleotides for the promotion of glycine, glutamic acid or leucine incorporation, but different fractions are required in each case. The fractions involved in the incorporation of glutamic acid and leucine have been tentatively identified as GU_2 and AU_2 respectively. Work is proceeding on the identification of fractions involved in promotion of the incorporation of other amino-acids.

It is clear that incorporation reactions for specific amino-acids can be activated by specific combinations of nucleotides, and it is probable that the effect of ribonucleic acid lies in the presence of these combinations within the polynucleotide structure. Since activation by whole ribonucleic acid appears to be species-

specific[1], it would follow that incorporation in species-specific proteins depends upon the order of these combinations of nucleotides in the corresponding nucleic acids, and that an experimental basis for something approaching a nucleic acid – template of the nature postulated by Dounce[3] and others is beginning to appear.

We are grateful to Dr. R. Markham for advice and guidance in separating and identifying nucleotide fractions.

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Anomeric Inversions by Glycosidases

β-AMYLASE has so far been considered a unique case among hydrolytic enzymes, as its action is accompanied by an inversion of the anomeric configuration of the splitting product produced; that is, β-maltose is formed from amylose, contrary to expectation. From our experiments it seems that two more glycosidases exist capable of analogous anomeric inversions.

Because of their close relationship to amylose, the following substrates were chosen, all three consisting of glucose chains with α-glucosidic linkages: (I) *cyclo*hexaglucan; (II) *cyclo*heptaglucan; (III) maltose.

The mode of action of takadiastase on all three substrates and of pancreatin on maltose was investigated (the *cyclo*dextrins are not attacked by pancreatin) with the following results.

(1) There are indications that two specific '*cyclo*dextrinases' ('*cyclo*hexa-' and '*cyclo*hepta-glucanase') are present in takadiastase. By precipitating with ammonium sulphate it was possible to obtain five fractions (*A* to *E*, in order of increasing concentrations of ammonium sulphate) with varying ratios of activities (*R*) towards *cyclo*hexa- and *cyclo*hepta-glucan as shown in Table 1.

(2) These '*cyclo*dextrinases' are not identical with either taka-amylase or takamaltase. Table 1 reflects also non-parallel variations and partial separation of the respective activities towards starch, maltose and the *cyclo*dextrins.

Table 1. Activities of takadiastase fractions obtained by precipitating with increasing concentrations of ammonium sulphate and dissolving the precipitates in equal volumes of water. The table includes a fraction *A* which was obtained in a different set of experiments. The activities are expressed in terms of initial drop in optical rotation per min. per ml. enzyme fraction, the activity of the original takadiastase arbitrarily taken as 100. *R* = ratio of activities towards *cyclo*hexa- and *cyclo*hepta-glucan

		Fractions					Orig. takadiastase
		A	*B*	*C*	*D*	*E*	
Activity towards	starch	23	36	33	33·5	27	100
	maltose	0	0	0	0	63	100
	*cyclo*hexaglucan	0	25	70	45	2	100
	*cyclo*heptaglucan	0	13	27	21	15	100
R			1·9	2·6	2·2	0·134	1

Table 2. Maximal mutarotations during enzymatic hydrolysis of *cyclo*dextrins and maltose by takadiastase and pancreatin respectively. Italic figures for rotation after addition of alkali

Enzyme / Substrate	Takadiastase *cyclo*Hexaglucan	Takadiastase *cyclo*Heptaglucan	Takadiastase Maltose	Pancreatin Maltose
Initial rotation	+4·86° *+4·89*	+1·09° *+1·07*	+3·57° *+3·56*	+2·89° *+2·87*
Rotation at stage of maximal mutarotation	+4·06 *+4·16*	+0·72 *+0·61*	+3·32 *+3·41*	+2·68 *+2·51*
Final rotation	+2·03 *+2·01*	+0·37 *+0·37*	+2·59 *+2·59*	+1·27 *+1·26*
Value of maximal mutarotation	+0·10	−0·11	+0·09	−0·17

(3) Calcium ions are specific activators of the two '*cyclo*dextrinases'. The activity of takadiastase towards the two *cyclo*dextrins was considerably weakened by dialysis against distilled water (but not against tap water). The original activity could be restored by addition of either tap water or 0·1 *N* calcium salts. The calcium ions could also be replaced by strontium ions for reactivation. The activity could not be restored by addition of the following ions also present in tap water: phosphate, sulphate, chloride, hydrocarbonate, magnesium, ferrous iron and sodium.

The mutarotations observed during the enzymatic hydrolysis of the two *cyclo*dextrins and of maltose by takadiastase and pancreatin respectively are summarized in Table 2.

Addition of alkali served to stop the hydrolysis at any stage and to accelerate the mutarotation of the sugars so far liberated[1]. Accordingly, the values "after addition of alkali" represent the rotation after attaining mutarotational equilibrium of the splitting products.

(4) Upward mutarotation was observed during the action of takadiastase on *cyclo*hexaglucan though the original substrate contains no β-glucosidic linkages.

(5) Downward mutarotation was observed during the action of takadiastase on *cyclo*heptaglucan according to expectation.

(6) Downward mutarotation was observed during the action of pancreatin on maltose, corresponding to liberation of α-glucose in accordance with expectation.

(7) Upward mutarotation was observed during the action of takadiastase on maltose, corresponding to liberation of β-glucose, contrary to expectation.

Observations (4) and (7) suggest that anomeric inversions are brought about by the two glycosidases involved (takamaltase and '*cyclo*hexaglucanase') concomitantly with their hydrolytic action, in analogy with the inversion observed with β-amylase.

I hope to publish a full account of this work elsewhere, together with Dr. J. Leibowitz, of Jerusalem, to whom I am indebted for help and advice. A part of this work was supported by a British Council Scholarship.

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Paper Electrophoresis of a Purified Specific Antibody

Recently, several workers[1] have tried to fractionate gamma-globulins and immune sera by electrophoresis. Such experiments have only given the mean properties of all gamma-globulin proteins, since non-antibody as well as antibody proteins occur in immune sera. We have now carried out paper electrophoresis of a purified specific antibody.

Antigenic azo-globulin was prepared by isolating pseudoglobulins from beef serum using ammonium sulphate[2], and coupling with diazotized anthranilic acid. Four rabbits were immunized as previously described[3], and, when a high antibody titre was established, these were killed by exsanguination and antibody precipitated from the antiserum with homologous antigen. The antibody was separated from the complex using sodium chloride solution and 0·1 *N* hydrochloric acid, as previously described[4], and the antibody estimated by micro-Kjeldahl nitrogen determination. Paper electrophoresis was carried out with a Jouan Paris, model 1603, apparatus and No. 204 papers measuring 400 mm. × 27·5 mm. Alkaline conditions (300 V., 100 m.amp., 6 hr., with a veronal–sodium veronal buffer, *p*H 8·8) and acid conditions (200 V., 100 m.amp., 5 hr., with a sodium veronal–acetate buffer, *p*H 4) were both used[5]. In each experiment we ran one strip with 0·1 ml. normal human serum as a control, and two strips with 0·05 ml. of antibody solution (825 mgm. protein/100 ml.). After electrophoresis, the strips were dried at 90°, stained for 15 min. in a bromphenol blue solution (0·2 gm. dye and 65 gm. mercuric chloride in 200 ml. 96 per cent ethanol), washed in tap water and dried at 100°. Colour intensity was measured with an optical densitometer. Pure antibody showed a single homogeneous peak at both acid and alkaline *p*H, corresponding at alkaline *p*H to the peak of the serum gamma-globulin.

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Neuromuscular Block caused by Acetylcholine

It has long been known that large doses of acetylcholine may cause a neuromuscular block[1]. This block has been thought to be due to the ability of acetylcholine to depolarize persistently the end-plate regions of the muscle fibres[2]. No direct studies on the relation of such a neuromuscular block to the muscle membrane potential have, however, been carried out.

In the present investigation this relationship has been studied on the sartorius nerve – muscle preparation of the frog (*Rana temporaria*). The membrane potentials and the end-plate potentials of single muscle fibres were recorded with capillary microelectrodes of external tip diameter less than 0·5μ filled with 3 *M* potassium chloride (for details of technique see ref. 3).

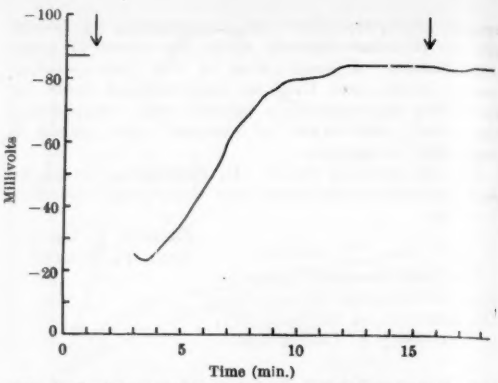

Fig. 1. Continuous registration of the membrane potential at the end-plate region of a single muscle fibre. At the arrows, acetylcholine iodide was added to the muscle bath, giving a concentration of 10×10^{-6} and 20×10^{-6} *M*

In the presence of 1×10^{-6} *M* neostigmine bromide, acetylcholine iodide (Hoffmann–La Roche) in a concentration of $5–20 \times 10^{-6}$ *M* caused a neuromuscular block. When the initial fibrillary twitches of the muscle fibres had subsided (about 60 sec.), the tip of the microelectrode was re-inserted at the end-plate region of a single muscle fibre and the membrane potential continuously recorded. These concentrations of acetylcholine caused a considerable reduction of the membrane potential at the end-plate region. Without removal of the acetylcholine the depolarization, however, spontaneously subsided and the membrane potential was restored to its original value within 7–15 min. as shown in Fig. 1. A subsequent addition of acetylcholine to the bath did not significantly change the membrane potential.

During the period of depolarization, a neuromuscular block developed and persisted despite repolarization of the membrane to the normal level. End-plate potentials could sometimes be recorded during the phase of depolarization, but never in the later phase when the membrane potential again was normal. The neuromuscular transmission remained completely blocked so long as acetylcholine was in the muscle bath and could only be restored slowly by washing the muscle in Ringer's fluid for 15–45 min. During the period of washing, the membrane potential remained normal and, preceding the relief of block, end-plate potentials again appeared. These end-plate potentials were markedly increased in size by repetitive stimulation of the motor nerve, and eventually an action potential could be elicited (Fig. 2).

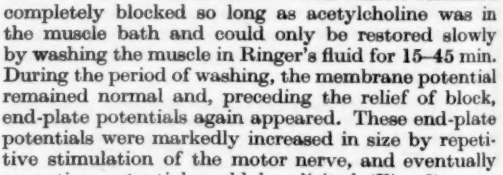

Fig. 2. (1) End-plate potentials have disappeared during the later phase of the neuromuscular block caused by 10×10^{-6} *M* acetylcholine iodide. (2) After washing the muscle with Ringer's fluid, end-plate potentials are recorded which are increased in size by repetitive stimulation of the motor nerve and which may lead to an action potential. (3) Time, 5 m.sec.

In the absence of neostigmine, a qualitatively similar neuromuscular block was caused by acetylcholine in about ten times higher concentrations. The observed changes of the membrane potential were only seen at the end-plate region and not in the nerve-free part of the muscle fibre. Concentrations of choline corresponding to the amounts of acetylcholine used had no detectable influence on the membrane potential or on the neuromuscular transmission.

It is concluded that prolonged neuromuscular block caused by acetylcholine in the sartorius muscle of the frog is not due to a persistent depolarization of the end-plate regions or of the adjacent membrane of the muscle fibres. The block is, on the contrary, characterized by a decreased sensitivity of the end-plate regions to the transmitter substance.

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Palatability of N-Oxides of Pyrrolizidine Alkaloids as a Factor in *Senecio* Poisoning

Recent chemical studies revealed that pyrrolizidine alkaloids are accompanied in the plants by their N-oxides[1]. In young growing plants, N-oxides may constitute more than 90 per cent of the alkaloid content, while in the autumn the proportion may be reversed[2].

Plants containing pyrrolizidine (*Senecio*) alkaloids have long been known to be responsible for poisoning livestock when present in pastures in various countries[3]. How the poisoning occurs is obscure, as animals usually refrain from eating poisonous plants. However, Theiler observed horses to consume fair amounts of *Senecio* plants in early spring.

During experimental studies on the induction of liver cirrhosis and primary liver tumours in rats treated with various *Senecio* alkaloids[4], administration of retrorsine, and of its N-oxide, isatidine, in drinking water disclosed a striking difference in the palatability of these two compounds. While rats abstained from drinking solutions of retrorsine containing more than 0·03 mgm./ml., they readily consumed tenfold more concentrated solutions of isatidine. As a result, high incidence of morbidity and mortality was observed among the young rats in the isatidine series, even though the isatidine treatment was discontinued after three weeks[5].

Isatidine acts insidiously, and may induce pathological changes several weeks or months after its administration. The following example illustrates this delayed action. Four young rats, weighing 65–70 gm., were injected intraperitoneally with isatidine, 4, 10, 28 and 40 mgm. per rat respectively. All survived at least four weeks, though the rats which received the two higher doses grew rather slowly, became anæmic and listless. The rat which received 40 mgm. of isatidine in a single dose died on the thirtieth day after the injection. It had œdema of the subcutaneous tissues, a pale, enlarged, fatty liver, and also pathological changes in the lung, spleen and pancreas. The rat which received 28 mgm. of isatidine developed bronchopneumonia, and was killed when *in extremis* on the forty-ninth day after the injection. It was very emaciated (weighed 90 gm.), had a dark, mottled, granular liver showing hæmorrhage and early fibrosis, and much hæmosiderin in the Kuppfer cells; œdema of pancreas; congested lungs with brown hæmorrhagic petechiæ, and some pathological changes in the spleen and kidneys. These organs as well as the mesenteric hæmolymph nodes gave a positive Prussian-blue reaction for iron-containing pigment. The two rats injected with the smaller doses of isatidine did not develop pathological changes during four months following the injections. Young rats similarly injected with retrorsine (5–15 mgm./rat) died in the course of one to three days after the injection, showing predominantly necrotic and fatty changes in the liver; some had hæmorrhage into the stomach and small intestines.

These experiments seem to indicate that when young growing plants contain pyrrolizidine alkaloids in the form of N-oxides, they would be palatable and readily consumed by livestock, which may afterwards develop various pathological changes depending on the time of survival.

It remains to be shown whether the delayed pathological changes result from the action of the N-oxides as such, or from that of the respective alkaloids into which they may be converted by reduction in the animal body.

I am indebted to Prof. F. L. Warren, Chemistry Department, University of Natal, Pietermaritzburg, for a gift of pure crystalline retrorsine and isatidine, and to Dr. M. A. Head for the microscopic evaluation of the pathological changes in the organs. My thanks are due to the British Empire Cancer Campaign for a grant.

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Antibody Formation in Humans against their own Stored Red Cells

In the course of a study on factors that may be involved in the *in vivo* destruction of stored red cells, an experiment was performed which suggests that the antigenicity of red cells is altered when blood is kept for a long period of time under standard storage conditions, and individuals may be sensitized with such stored red cells.

In order to facilitate the presentation of the experimental work, the time of starting the experiment will be designated 'day 0' and the various operations will be referred to the starting day. 125 ml. of blood was withdrawn into 'Baxter'[1] bottles from ten healthy individuals ranging in age

from twenty-one to thirty-two years. 10 ml. in addition were withdrawn at this time and the serum separated. The blood stood 42 days. During the course of a three-week period following the storage interval, six intravenous injections of 7-ml. quantities of the blood, two injections per week, were made into the individuals from whom the blood was obtained; that is, each individual was injected with his or her own stored blood. Ten days after the last injection (day 70) 20 ml. of blood was withdrawn from each individual; 10 ml. was placed in a bottle containing *ACD* solution, and the serum was separated from the remainder. Additional samples of blood were withdrawn and placed in *ACD* solution as the work continued. The blood in *ACD* solution was kept at 3° ± 1° C. and the serum samples were frozen at − 18° C. The blood samples were prepared and handled using precautions to ensure sterility, and no contamination was detected during the course of the experiment. Red cells were obtained for testing by removing some blood from the storage bottle just before a test was carried out, washed three times in saline buffered at *p*H 7·3, and made up to a 1 per cent concentration.

Between days 71 and 77 the following tests were carried out using day 70 serum and day 0 and 70 red cells of the same individual: agglutination tests using saline and serum as diluents, and cells that had been treated with trypsin; hæmolysis test with added complement; and the Coomb's test with normal and trypsin-treated cells (Coomb's test repeated on day 164). All the tests were negative. A short while later, the opportunity of utilizing the erythrophagocytic test[2] was made available. In this test the mixture of red cells and serum is added to a slide culture of phagocytic cells obtained from rabbit spleen. After a 30-min. period, fifty phagocytic cells are observed, and the percentage of them which have ingested red cells is referred to as the phagocytic index. Under normal conditions this ranges up to about 10; but when the red cells are sensitized by antisera, it is increased to 25 or more. The results cited were obtained on day 127. In six of the ten individuals, there was a significant increase in the phagocytic index when day 70 serum was mixed with old (day 0) red cells. There was no such increase when day 70 serum was mixed with fresh red cells, or when day 0 serum was mixed with old or fresh red cells. When day 70 serum was absorbed with old and with fresh red cells (one volume of serum plus one volume of the respective cells), the phagocytic index was markedly decreased after the single absorption with old red cells but was unchanged after absorption with fresh cells. The results obtained with old red cells are presented in Table 1. These results suggest that these six individuals produced antibodies against their own stored red cells.

The antigenic change in stored red cells may be due to an enzyme or enzymes in the blood, perhaps on the red cell itself, that acts on the red cell. The reason why positive results were obtained only with the erythrophagocytic test may be due to (1) the decreased ability of old red cells to react in some serological tests, (2) the production of small amounts of antibody with the particular injection procedure used, and (3) the possibility that the reaction can be detected only with a particular type or types of serological tests. These and related questions are under investigation.

If individuals can be sensitized with stored red cells, the problem of sensitization may have to be considered in investigations directed toward preserving blood for longer periods of time than is possible at present. If, for example, a way is found of preserving blood for transfusion for two- or three-month periods and the antigenic changes are not inhibited, the recipient of the old blood may become sensitized to it and have a transfusion reaction with subsequent transfusions of old blood.

Table 1. Phagocytic Indices of Stored (Day 0) Red Cells with Sera

Cells and serum of the same individual were tested. The phagocytic index recorded is the average of duplicate tests, both of which were in the same range in all cases

Experimental subject	Normal rabbit serum*	Serum obtained at start of experiment (day 0)	Serum obtained after injection procedure (day 70)	Day 70 serum absorbed with day 0 red cells	Day 70 serum absorbed with fresh red cells
Increased P.I.					
M. S.	4	13	29	14	22
G. G.	8	3	34	17	31
M. M.	12	9	22	3	25
J. H.	6	0	27	8	23
L. C.	10	6	30	13	22
R. S.	13	5	28	16	28
Average	9	6	28	12	25
No increase in P.I.					
K. R.	3	10	12	7	1
G. W.	7	13	1	4	9
L. N.	1	6	6	5	2
R. B.	9	13	9	11	10
Average	5	10	7	7	5

* Used as a control

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[1] This is the 125-ml. size of a type of bottle in routine use for storing blood. Contained 40 ml. of *ACD* solution of following compositions: 1·38 gm. dextrose, 1·24 gm. sodium citrate and 0·45 gm. citric acid per 100 ml. Manufactured by Baxter Laboratories, Morton Grove, Illinois.

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Coagulation Mechanism of the Horse

An investigation has been made, by means of the newer coagulation tests, into the coagulation mechanism of horses' blood. As compared to human values, the most striking features are the greatly prolonged clotting time, poor clot retraction in spite of a platelet count within normal human limits and a prolonged one-stage prothrombin time.

Using the thromboplastin generation test[1], the prolonged clotting time was found to be due to a deficiency of antihæmophilic globulin, and this defect was present in both sexes. The deficiency was corrected by normal human plasma. This finding may well prove a most useful tool for those investigating hæmophilia in man. The horse is the only known animal exhibiting this defect, which is a species difference of great interest.

A full report of these findings will be published in due course elsewhere.

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Pseudocholinesterase in Pacinian Corpuscles

We have recently studied the distribution of cholinesterases in the cat's pancreas by Koelle's histochemical method[1], and observed that among other structures which contain enzyme the Pacinian corpuscles are prominent. The cholinesterase was seen to be concentrated in the core and stalk of this sensory organ (Fig. 1). By the use of appropriate substrates (acetyl- and butyryl-thiocholine) and a selective inhibitor (di*iso*propyl-fluoro-phosphate) the enzyme has been identified as pseudocholinesterase. Although the Pacinian corpuscles found in this situation are not pancreatic structures, being part of the enfolding mesentery, their location here is convenient because it is easier to section them when supported by the glandular tissue than when they are lying free in the mesentery.

So far as we are aware, the presence of pseudocholinesterase in Pacinian corpuscles has not previously been reported. Other nerve structures known to contain the enzyme are glial cells and the nuclei of certain ganglion cells[1,2]. There is no reason for supposing that the enzyme is concerned in acetylcholine hydrolysis in the Pacinian corpuscles[3] or at any of the other sites mentioned. It may be of importance, however, for the metabolism of the nerve tissue with which it is associated; and in this one structure which can be studied as an independent unit a means of testing this hypothesis is provided. It is not necessarily to be expected that inhibition of the enzyme (by, say, di*iso*propyl-fluoro-phosphate) would produce immediate effects; but given *in vivo* over long periods, its excitability should certainly show a change if pseudocholinesterase has any important place in the function of nerve tissue. These considerations may be of importance in interpreting the biochemical lesions produced by anticholinesterases[4].

We are indebted to Mr. G. Bull for the photomicrographs.

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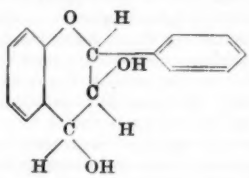
Formation of Leuco-Anthocyanins in Eucalypt Tissues

Robinson and Seshadri have postulated that C_6—CH(OH)—CH(OH)—CH(OH)—C_6 is the form of the precursor of the various classes of anthoxanthidins, and the anthocyanidins (for discussion, see ref. 1). Recent work[2] has shown that the leuco-anthocyanidins have the cyclic form of this structure:



so that this class could be one of the first forms of polyphenolic compounds synthesized in the plant and be the precursor of the above substances as well as catechins and tannins. If this were so, one would expect appreciable amounts of leuco-anthocyanins to be formed in areas of intense metabolism.

It has been possible to test this hypothesis by the examination of young leaves and of the cambial region of certain eucalypts. In the late spring and early summer the first-formed leaves of many young eucalypt stems are red to red-brown. Such leaves at various stages of development from several species, including *Eucalyptus sieberiana* F. Muell., *E. elaeophora* F. Muell., *E. regnans* F. Muell., *E. obliqua* L'Hérit. and others, were examined. The youngest leaves were completely red except for the extreme tip, which was pale green and is probably the area of most active cell division. The body of the leaves contained anthocyanins and also appreciable quantities of leuco-anthocyanins, but the greatest amount of the latter was found

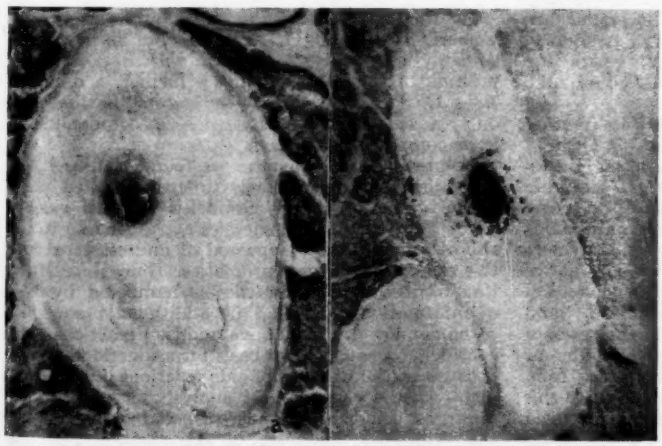


Fig. 1. Two sections (20μ), at different levels, of a Pacinian corpuscle from a cat's pancreas. (*a*) Incubated with butyrylthiocholine in the presence of 10^{-7} *M* di*iso*propyl-fluoro-phosphate. (*b*) Incubated with butyrylthiocholine alone. In (*a*) there is no evidence of enzyme activity. In (*b*) the much more darkly staining core shows deposits of copper sulphide where hydrolysis of the substrate has occurred

in the tips. The disappearance of the anthocyanin from the leaf and decrease of leuco-anthocyanins in the extreme tip appeared to occur simultaneously. The leuco-anthocyanin was always present in the leaves but decreased in amount as the leaves aged. Green areas appeared on either side of the mid-rib as the leaves became more mature. The red material (and probably the leuco-anthocyanin) was apparently transported elsewhere by means of the veins, which became noticeably red; but finally they, too, became green. The intensity of the red of the bark of the twigs to which the leaves were attached reached a maximum when the leaves became entirely green.

Another area of intense cell division and expansion is the cambial region. Again the hypothesis held, since in a log of *E. regnans* from which the bark was slipped readily, considerable amounts (1·3 per cent) of leuco-anthocyanidin were found in the cambial region; the phloem contained 1·8 and the sapwood 0·04 per cent. After the spring flush of growth had passed, leuco-anthocyanins were difficult to detect in the cambium.

In most tree species, the change of sapwood to heartwood is usually abrupt, and there is practically always a change in the colour of the wood and an increase in the amount and colour of the extraneous materials present in the cavities of the various cells, particularly the rays and vertical parenchyma cells. The heartwood is usually uniform, but occasionally samples of a species show a distinct outer heartwood zone (up to 1¼ in. wide); although this zone contains the same amount of total extractives, their properties differ from those of the inner heartwood. One theory of heartwood formation considers that the extractives are formed during the sudden burst of cell activity at the boundary between the sapwood and heartwood. In order to learn whether leuco-anthocyanins are formed in this region as they were in areas where cell division occurred, several cross-sections of jarrah (*E. marginata* Sm.) were examined. Sections 30μ thick were taken every 1 cm. or less across the samples and analysed. An increase in leuco-anthocyanin occurred at the boundary; but instead of a temporary increase the value remained fairly constant across the outer heartwood zone, after which there was a steady decrease. Consequently it seems unlikely that the leuco-anthocyanins are synthesized at the sapwood–heartwood boundary, but are translocated to this locality, where the final changes to heartwood extractives would take place.

The leuco-anthocyanins were estimated by treating with propanol : 3 *N* hydrochloric acid (5 : 1) in a closed tube and determining the resulting anthocyanidin[3]. The anthocyanins present in the leaf were estimated separately. This method of detecting leuco-anthocyanins was more sensitive than methods which involve heating in an open vessel and more particularly those using aqueous acid. The above method has shown that mixtures of leuco-anthocyanins often occur in the tissues examined; and also by using standard conditions different rates of red colour formation have been shown by different raw materials. When pure leuco-anthocyanins from *Acacia melanoxylon* heartwood were subjected to this treatment and the transformation products examined by paper chromatography, these showed the presence of 3,3′,4′,7,8 pentahydroxy flavylium chloride, 3,3′,4′,7,8 pentahydroxy flavone, a substance which could be the undescribed 3,4′,7′,7,8 pentahydroxy flavane and other substances. The formation of similarly related compounds by different acid treatments of leuco-anthocyanidins have been reported[4]. The extent to which the leuco-anthocyanin is converted to anthocyanidin, anthoxanthidin, catechin or tannin appears to depend on the extent of oxidation in the *in vitro* system. The different responses of different leuco-anthocyanins to such conditions may explain why unrelated members of these different classes are finally found in plant tissues.

Fuller details of this work will be presented elsewhere.

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Relative Reactivities of Substituted Anthracenes towards the Addition of 2-Cyano-2-propyl Radicals

2-Cyano-2-propyl radicals generated by thermal decomposition of azo-bis*iso*butyronitrile in benzene solution readily add on to the *meso*-positions of anthracene[1] or substituted anthracenes[2] to form substituted 9,10-dihydroanthracenes. The following reactions take place (R = 2-cyano-2-propyl; A = anthracene):

$$R-N=N-R \xrightarrow{k_a} N_2 + 2R. \qquad (a)$$

$$R. + A \xrightarrow{k_b} R-A. \qquad (b)$$

$$R-A. + R. \xrightarrow{k_c} R-A-R \qquad (c)$$

$$R. + R. \xrightarrow{k_d} R-R \qquad (d)$$

In the case of unsubstituted anthracene, two isomeric compounds $R-A-R$ are formed, presumably a *cis* and a *trans* form with respect to the position of the two R groups; further, a dimer of $R-A.$ is obtained. With 9-substituted anthracenes, only a single isomer $R-A-R$, probably the *trans* compound, is formed.

In previous experiments[3] we found that the rate of addition of free radicals to unsubstituted polycyclic aromatics closely paralleled the free valence numbers or localization energies corresponding to the site of attack, and it appeared of interest to extend this work to substituted aromatics. Here, the calculation of theoretical quantities is hampered by lack of information regarding the additional parameters to be employed. The above addition reactions were considered a satisfactory basis for a kinetic approach because of the absence of side-reactions; moreover, ultra-violet spectroscopical analysis of the reaction mixtures could be considered possible in view of the benzenoid character of the reaction products $R-A-R$, as the anthracenes absorb at longer wave-lengths and have higher extinction coefficients than the former.

If a large excess of azo compound is used, the concentration of $R.$ will be mainly determined by the rate of decomposition of the azo compound and the rate of dimerization of $R.$ (equations a, d).

For steady-state conditions we can derive the approximate equation,

$$\ln \frac{A_0}{A_t} = k_b\left[k_a^{1/2}\, k_d^{-1/2} \int_0^t (B)^{1/2}\, dt\right]$$

in which (A_0) and (A_t) are the anthracene concentrations at times zero and t, respectively, and (B) is the concentration of the azonitrile. The term in brackets is independent of the anthracene. Using the same intake of azo compound, the ratios of ln (A_0/A_t) for various anthracenes after the same time-interval afford relative values for the rate constants of addition, k_b.

The experiments were carried out in methylcyclohexane solution. After thorough degassing, ampoules containing $\frac{1}{2}$–1 mgm. of the anthracene and 10–30 mgm. of azobis*iso*butyronitrile in 25 ml. of solvent were sealed under pure nitrogen. A method was developed for accurately determining anthracene concentrations directly in the ampoules by means of ultra-violet spectrophotometry, using standard curves and background corrections at two or three wave-lengths. In runs at 55° C., anthracene concentrations were determined at twelve time-intervals over a period of about 500 hr., in runs at 70° C. after 18 and 64 hr. The half-life of the azo compound is about 47 hr. at 55° C. and 5 hr. at 70° C. Anthracene conversions were in most cases 40–60 per cent.

The ratios of the k_b values appeared to be practically constant, a fact supporting the assumed kinetics. The spectroscopical accuracy of the anthracene determinations was about 2 per cent, which leads to a mean error in the k_b values of about 0·02. Mean deviations from constancy in the k_b ratios were about 0·03; for the unreactive compound 9,10-dimethylanthracene and the highly reactive 9-cyanoanthracene, the results are believed to be reliable to within 0·06 and 0·25 respectively. Mean relative rate constants based on an anthracene value of 2·00 are given in Table 1.

Substituent influences are seen to be generally small, a fact which is in agreement with Coulson's conclusion[4] that substituents have little influence on free valence numbers or localization energies, particularly when present at other than the *meso*-positions.

Table 1. Relative Rate Constants for Free Radical Addition

Anthracene*	Relative rate constants			
	55° C.		70° C.	
	Total	For 10-position†	Total	For 10-position†
Unsubstituted	2·00	1·00	2·00	1·00
2-Methyl	2·00	1·00	—	—
9,10-Dimethyl	0·24	0·12	0·42	0·21
9-Methyl	2·12	2·06	2·16	2·06
9-Ethyl	1·54	1·48	—	—
9-Cl	1·70	1·64	1·72	1·62
9-Br	1·39	1·33	1·38	1·28
9-OCH_3	2·15	2·09	2·16	2·06
9-CN	4·30	4·24	4·04	3·94

* Synthesized by standard procedures and purified by percolation over silica gel and repeated crystallizations.

† Computed on the assumption that additions at positions carrying a substituent should be very slow. Thus, in 9-methylanthracene the 9-position should be about one-half as active as in 9,10-dimethylanthracene, that is, 0·06 (55° C.) or 0·10 (70° C.). For the other 9-substituted compounds the contributions of the 9-positions were also taken to be 0·06 and 0·10.

Reactivities depend largely on the conjugative effect of the substituents, polar influences being apparently unimportant. The same conclusion was drawn by Hey *et al.*[5] on the basis of phenylations of benzene derivatives; here, partial rate factors for *p*-NO_2, *p*-Cl, *p*-Br and *p*-CH_3 were found to be 7·9, 1·2, 1·8 and 1·4 (D. H. Hey, personal communication), respectively. The value for 9-cyanoanthracene is slightly higher than that found earlier for CCl_3 radicals at 90° C. (2·8)[6].

Steric influences on conjugation appear to affect the reactivities of anthracenes carrying a bulky 9-substituent. Thus, contrary to the small linear cyano group, the methoxy group is prevented from assuming co-planarity with the rings by the 1 and 8 hydrogen atoms[7]; the conjugating effect of the methoxy group is thereby decreased to the level of the methyl group. The low value found for 9-ethylanthracene as compared with that of the 9-methyl derivative indicates that hyperconjugation is less pronounced in the former case; however, since this was to be expected even if the ethyl group were not hindered[8], our result cannot be considered a convincing proof for steric interference with hyperconjugation in 9-ethylanthracene. The lower value found for 9-bromo- as compared with 9-chloroanthracene is in contrast to the order found for phenylation of benzenes; this may be related to the greater bulkiness of Br as compared with Cl.

The above conclusions are believed to be independent of the assumptions made as regards the contributions of the 9-position, differences between the various total reactivities being appreciable.

The temperature coefficients of the relative reactivities are probably small. Since analogous 10-positions are attacked, it seems plausible to attribute differences in relative reactivities at a given temperature solely to differences in activation energies. This would lead to differences between the values at 55° and 70° C. of only a few per cent; the general trend of data is therefore consistent with this view.

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Use of 'Dieldrin' to protect Wool against Insect Attack

The problem of protecting wool from insect attack has received considerable attention in the past. Methods of temporary protection are available using insecticides such as silico-fluorides, DDT and 'Gammexane'; but these are not fast to processes

such as continued washing or dry-cleaning. Several types of chlorinated aromatic sulphonic acids are commercially available which combine with wool from the dye-bath to give a satisfactory permanent result[1]. The industrial application of such methods has been limited, due probably to the fact that the amounts required (at least 1 per cent of the weight of wool) can result in a treatment which is considered to be too expensive.

In experiments to ascertain the effectiveness of 'Dieldrin' and 'Aldrin' for these purposes, it has been observed that 'Dieldrin' in low concentrations is a most effective mothproofing agent, producing a result which is unexpectedly fast to both washing and dry-cleaning.

Samples of worsted fabric (4 gm.) were treated with petroleum ether solutions of each insecticide, the amount applied being regulated by the weight of solution taken up by the sample. After each treatment, the solvent was removed by evaporation at room temperature. To assess washing fastness, each sample was washed in a wash-wheel using 120 ml. of 0·2 per cent soap solution at 45° C., the solution being renewed every 15 min. To determine the effect of dry-cleaning, a sample was placed in a jar with 120 ml. white spirit and rotated for the required time, the solvent being renewed every 15 min.

The effectiveness of each treatment against clothes moth (*Tineola bisselliella*) was evaluated by exposing each of four samples of the various fabrics to ten larvæ for a period of fourteen days and observing loss in weight of fabric and mortality of larvæ.

The results, which will be reported in detail elsewhere, show that 0·05 per cent 'Dieldrin' on the weight of wool gives a mothproof effect which persists after 1½ hr. washing and 1 hr. dry-cleaning.

Preliminary experiments indicate that 'Dieldrin' is also very effective against furniture carpet beetle (*Anthrenus flavipes* Le Conte). As application from aqueous suspension gives similar results, the method offers the possibility of a convenient technique for protecting wool against insect attack.

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Tanning of Blowfly Puparia

The nature of the aromatic component responsible for the tanning of the cuticle of blowfly puparia is not entirely clear. Pryor, Russell and Todd[1] isolated protocatechuic acid from puparia of *Calliphora erythrocephala*, but could not find any phenolic material in *Lucilia caesar*. They used large quantities of insects preserved in sulphur dioxide solution. I have re-investigated the problem on small quantities of fresh material, using paper chromatograms.

With *m*-cresol – acetic acid – water solvent, and developing with ferric chloride, small concentrations of dioxyphenylalanine were found in mature larvæ of *Calliphora* and *Lucilia*, but no protocatechuic acid, although by the same method it was possible to demonstrate the presence of protocatechuic acid in fresh oothecæ of *Periplaneta* and of 3·4 dihydroxyphenylacetic acid in preserved imagines of *Tenebrio molitor* and *Sitophilus granarius*. Besides dioxyphenylalanine, *Calliphora* extracts showed the presence only of two substances giving a colour with ferric chloride; one, pink, at R_F 0·54, and another, a brownish-pink, at R_F 0·75. Repeating the experiment with butanol – acetic acid – water as solvent, and developing with Ehrlich's reagent, ninhydrin, diazotized sulphanilic acid, and ferric chloride, these spots were shown to be due to kynurenin and 3-oxykynurenin; compared with authentic samples they showed the same R_F values, gave the same colours with the various developers, and showed the same fluorescence in ultra-violet light. Both substances are present in relatively high concentration.

A comparison with Levenbook's[2] findings on the blood of *Gastrophilus intestinalis* suggests that the unknown aromatic amino-acid which he found to be present in high concentration was in fact 3-oxykynurenin. Levenbook suggested that his unknown amino-acid was important for the hardening of the puparium, and the behaviour of 3-oxykynurenin with extract of larval cuticle confirms this. When incubated in a respirometer with cuticle extract at *p*H 7·0, 3-oxykynurenin absorbs oxygen nearly as fast as an equimolar concentration of catechol under the same conditions.

These preliminary observations suggest that in *Calliphora*, and probably in other insects, there is an alternative method of tanning the cuticle, using aminophenols derived from tryptophan instead of dihydroxyphenols derived from tyrosine. Butenandt *et al.*[3] have shown that insect eye pigments, as well as the insectorubins described by Goodwin[4], are formed by the condensation of two molecules of 3-oxykynurenin; it is tempting to suppose that the formation of these pigments is a byproduct of a mechanism for tanning the cuticle.

I am indebted to Dr. C. E. Dalgliesh for specimens of kynurenin and 3-oxykynurenin.

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Cytological Contributions to the Phylogeny and Classification of the Rodent Genus *Gerbillus*

The Gerbillinae are highly differentiated rodents exhibiting many instances of parallel specializations in external and anatomical features evolved in independent lines. Consequently, the present state of the taxonomy of this group is unsatisfactory. Three years ago we started an extensive study of the chromosome complements in the species occurring in Israel. The comprehensive cytological studies of Matthey[1,2] enabled us to compare the idiograms of our species with those of others from different parts of the family range.

Table 1

	Origin	2n (male)	Sex chromosomes	No. of metacentric chromosomes	No. of chromosome arms
Group *a*					
*Gerbillus gerbillus gerbillus**	Israel (Negev)	43	XY_1Y_2	38–40	81–83
Group *b*					
Gerbillus allenbyi Thomas	Israel (coastal plain)	40	*XY*	40	80
Gerbillus pyramidium	Algeria	40	*XY*	38	78
Gerbillus pyramidum	Israel (coastal plain)	52	*XY*	22–24	74–76
Gerbillus pyramidum	Israel (Negev)	66	*XY*	8–12	74–78
Group *c*					
Gerbillus (Dipodillus) nanus	Israel (Negev)	52	*XY*	10–14	62–66
Gerbillus (Dipodillus) dasyurus Wagner	Israel (various localities)	60	*XY*	6–8	66–68
Group *d*					
Gerbillus calurus Thomas	Israe (Negev)	38	*XY*	32–36	70–74

* Authors' names are omitted when the populations referred to cannot reasonably be supposed to correspond with the types on which the original description was based.

Table 1, which summarizes some of the karyological characters of the species currently considered to belong to the genus *Gerbillus*, reveals a great diversity in numbers and forms of chromosomes. Nevertheless, the forms studied may be arranged in four groups on the basis of chromosome morphology and evolution.

Group *a* includes so far only *G. gerbillus gerbillus*. Multiple sex-chromosomes, very probably of the XY_1Y_2 type, are readily recognizable as a trivalent in metaphase I (Fig. 2). The male diploid chromosome number is 43 (Fig. 1), whereas a single female examined was found to have almost certainly 42 chromosomes. The large and easily distinguishable *X*-chromosome is present twice in the female. Although this species has almost the same number of chromosomes and chromosome arms as *G. allenbyi* and *G. pyramidum* (Algeria), its metacentric chromosomes present a striking contrast to those of all other forms studied in being much shorter than the *V*-shaped elements of the other karyotypes. This unique character, which was observed in all plates, demonstrates clearly the caution required in evaluating the significance of the number of chromosome arms. It appears to us that both the detailed morphology and the gross differences in the size of the elements deserve consideration in comparative studies.

Since within groups *b* and *c* there is approximate correspondence in the size of the chromosomes and in the number of their arms, the wide variation in the mitotic numbers must be attributed to Robertsonian changes. Group *b* comprises four forms. The first is endemic to Israel and currently considered as the subspecies *allenbyi* of *G. gerbillus* Olivier[3]. There is no doubt that *G. allenbyi* shares the main karyological characteristics of the three other members of this group while presenting none of the cytological features described above for *G. gerbillus*. It must be concluded, therefore, that it can no longer be regarded as conspecific with *G. gerbillus*. We propose to restore the original author's name *G. allenbyi* Thomas 1918. The other three forms of this group, each of different geographical origin, have been provisionally designated as *G. pyramidum*, since for the present they can only be distinguished by their cytological characteristics. Dr. T. C. S. Morrison-Scott (personal communication), who kindly examined a few specimens from the three populations, came to the conclusion that those differences that "exist between the six specimens submitted are not such as would justify nomenclatural differentiation according to the normal criteria used in taxonomy. I should not have called them different races". It should be noted that *G. pyramidum* is sympatric with *G. allenbyi* in the coastal plain. We believe, therefore, the latter to be specifically different from the *pyramidum* complex in Israel. *G. pyramidum* from the Negev, the southern semi-desert of Israel, is of particular interest since it exhibits a chromosomal polymorphism the study of which is now in progress. Apart from the individuals possessing 33 bivalents, other specimens from the same locality were found to have only 31 autosomal elements in the first meiotic metaphase, one of them rather asymmetrical. This would seem to be the first record of an intrapopulational chromosomal polymorphism in mammals. Matthey's observation[1,4] of a multiple sex mechanism in *G. pyramidum* from Algeria could not be confirmed in the three Algerian specimens examined by us.

Group *c* includes *G. nanus* and *G. dasyurus*, which are very similar externally. Earlier taxonomists referred these species to the genus *Dipodillus*. Modern authorities considered the characters used for this separation to be of secondary value and therefore assigned only subgeneric rank to the *Dipodillus* group[5]. The cytological evidence favours the separate status of these species, since they are different from the other groups in chromosome size and number of arms. Like group *b*, they show a Robertsonian relationship among themselves. *G. campestris*, $2n = 56$, studied by Matthey[1], cannot be fully compared with the above species because no mitotic plates are figured. But the similarity in the aspect of the first metaphase plates would seem to confirm the affinity of this form to the *Dipodillus* group[3,5]. *G. nanus* ($2n = 52$) has a distinct sex bivalent, whereas the sex chromosomes could not be identified in *G. garamantis* ($2n = 54$)[3],

Fig. 1 Fig. 2

Gerbillus gerbillus gerbillus. Acetic-orcein squashes after hypotonic pretreatment. Camera lucida drawings. × 1,650. Fig. 1. Spermatogonial metaphase; chromosome *X* in outline. Fig. 2. Metaphase I; sex trivalent stippled

considered to be another race of the same species[3].

G. calurus (group *d*) has been assigned to the genus *Meriones*, although originally described as *Gerbillus calurus*[3]. Recently, it was referred once again to the subgenus *Dipodillus* by Wassif[6] on morphological evidence. The cytological picture does not warrant the inclusion of this species in the *Dipodillus* group. The mitotic plate somewhat resembles that of group *b*. However, cytological characteristics alone do not seem to suffice at the present stage to justify the establishment of a novel taxonomic grouping.

On the other hand, the findings reported here—which will be presented in full elsewhere—suggest that by applying comparative cytological methods it is possible to split artificial assemblages of forms. Moreover, in view of the cytological heterogeneity already recorded, we hope that a wide-scale study of the numerous gerbils known will contribute materially to the natural classification of this family.

The technique of pre-fixation treatment with diluted Tyrode solution was mentioned in an earlier note[7]. Excellent results are also obtained by the use of 0·3–0·5 per cent sodium chloride solutions. Three to seven males of each species were analysed.

We thank Dr. E. Goldschmidt for her interest in this work. We are indebted to Dr. T. C. S. Morrison-Scott for the identification of several specimens and to Dr. F. Petter for gerbils from Algeria. The animals used in this study were collected by Dr. H. Mendelssohn, Mr. M. Costa and ourselves during a survey of the rodents of Israel.

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Influence of Impurities on the Growth of Quartz Crystals from Flint and Quartzite

Hitherto the most successful methods[1,2] of growing large quartz crystals have employed a hydrothermal technique in which melting-quality quartz is used as the source material for maintaining the supersaturation of the liquid with respect to silica in the vicinity of the growing crystals. We have now found means whereby the melting-quality quartz can be replaced satisfactorily by other mineral substances rich in silica, such as flint and quartzite. These materials have the advantage of ready availability in the United Kingdom.

When flint, a cryptocrystalline variety of quartz, is used in place of melting-quality quartz without any other changes in the procedure previously described[2], the resulting crystals show minor but distinct changes in habit and a serious worsening of crystalline quality. However, we find that when the usual aqueous solution of sodium carbonate is modified by the addition of certain proportions of sodium hydroxide and sodium fluoride[3], crystals are obtained which are similar in quality and habit to those grown from melting-quality quartz.

Quartzites, as source materials, fall into two main classes. Class *A* behave much the same as melting-quality quartz, whereas class *B* require the modified solution referred to above. Considerable experimental evidence has been obtained to indicate that this difference is associated with the nature of the felspar which is commonly present as a minor constituent of the quartzite. Moreover, a preliminary investigation has shown that the poorer quality obtained from flint and class *B* quartzites, when crystals are grown in a sodium carbonate solution, is due to the incorporation of aluminium into the structure of the growing crystals. The evidence for this is provided by spectrographic tests, paramagnetic resonance experiments[4], and the study of the darkening brought about by X-ray irradiation of sections cut from crystals. In addition, the direct test has been made of deliberately adding aluminium in a number of forms to the solution when growing from pure melting-quality quartz. It is found that, in the presence of this aluminium, the system behaves as if flint or class *B* quartzites were being used, and the reversion to normal good quality is brought about by the use of the modified solution. This is illustrated by Fig. 1, in which the small experimental crystals shown were grown under the following conditions:

	Source materia	Solution
(*a*)	Flint	Sodium carbonate
(*b*)	Melting-quality quartz + aluminium	,, ,,
(*c*)	Melting-quality quartz	,, ,,
(*d*)	Melting-quality quartz + aluminium	,, ,, + sodium hydroxide + sodium fluoride

Although not illustrated, the crystals obtained from class *B* quartzites in sodium carbonate solution are similar to that shown in Fig. 1(*a*). In the same way, Fig. 1(*d*) is typical also of the crystals obtained from flint and class *B* quartzites using the modified solution. The feature of these crystals which is most readily apparent from the photographs is the nature of the upper surface, approximating to (0001), on which most growth takes place. The pronounced pitting of this surface in Figs. 1(*a*) and (*b*) should be contrasted with its smoothness in Figs. 1(*c*) and (*d*).

Fig. 1

It has been observed that the pitted crystals tend to develop cracks during their growth, and examination shows that they are in a state of strain.

The results obtained from flint and class *B* quartzites can be explained by the presence of small amounts of aluminium in the mineral which become available for incorporation in the growing crystal. In the quartzites, this aluminium will generally originate from the felspar in the rock. The most important feature requiring explanation is the difference between class *A* and class *B* quartzites. It is believed that this difference lies in the behaviour of various felspars under the hydrothermal conditions. In general, we have found that the aluminium present in the triclinic felspar minerals is bonded in the structure in such a way that the aluminium does not become available in solution in a form that results in its incorporation into the growing crystal. These are the felspars present in the class *A* quartzites. In contrast, the monoclinic felspars, in particular orthoclase in its various forms, break down so that the aluminium does become incorporated. This latter type of felspar is considered to be responsible for the behaviour of at least some of the class *B* quartzites. It appears probable that the behaviour of the two classes of felspars is related to the degree of ordering of the aluminium and silicon atoms in the crystal lattice, the aluminium in the disordered structures going into solution in a form which can be taken up in the growing crystal.

We acknowledge the advice and encouragement of Mr. J. W. Ryde throughout the course of this investigation. We are also indebted to Dr. W. H. Taylor for a helpful discussion regarding the felspar problem, and to Dr. J. H. E. Griffiths and his collaborators for information on paramagnetic resonance behaviour.

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Dielectric Properties of Pinacol Hydrate: Application to Temperature Measurement

In the course of research into the dielectric properties of hydrogen-bonded structures, the dielectric properties of pinacol hexahydrate $\{(CH_3)_2.C(OH).C(OH).(CH_3)_2.6H_2O\}$ were measured. It was found that in this compound a region of dielectric dispersion occurs centred about a frequency of 80 kc./s. at a temperature of 20° C. For polycrystalline material the relative permittivity falls from 45 to 3 in this dispersion region. The mid-frequency of this dispersion varies rapidly with temperature (Fig. 1) and can be described by the following expression: $f = 2 \times 10^{17} \exp(-H/kT)$ sec.$^{-1}$, where H is 16·5 k.cal./mol. In the vicinity of 20° C.

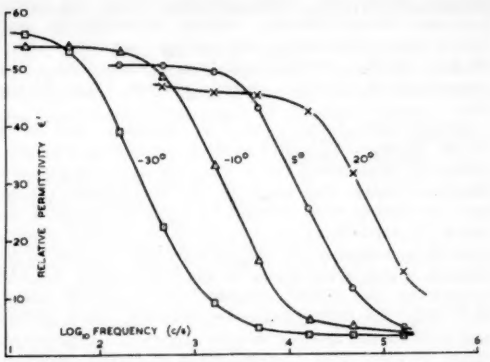

Fig. 1. Dielectric dispersion of pinacol hexahydrate at various temperatures

this means that the centre frequency of the dispersion region has a temperature coefficient $\left(\frac{df/dT}{f}\right)$ of 9 per cent per deg. C., and, if measuring at a fixed frequency near the centre, the variation in permittivity is 5·5 per cent per deg. C. The resistance of semiconducting material used in thermistors varies at the rate of 1·5–5 per cent per deg. C. at about room temperature[1]. Consequently it would appear that a capacitor made with pinacol hydrate as dielectric could have applications as the thermal-sensitive element in circuits used for the measurement or control of temperature.

There is, of course, dielectric absorption associated with this dispersion, with a maximum dielectric loss factor of 17 corresponding to a tan δ of approximately 0·75 at the centre of the dispersion region. However, in any application based on the rate of change of permittivity with temperature, provided the centre of the dispersion region is used, the change in dielectric loss factor will be small, since the absorption has a flat maximum in this region.

It should be mentioned that any capacitor constructed with pinacol hydrate would need to be sealed, since this compound loses moisture slowly on exposure to the atmosphere (approximately 20° C. and 60 per cent relative humidity) and reverts to pinacol.

A more complete discussion of the dielectric properties of this compound is in preparation.

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Pulsation and Mass Transfer of Pendent Liquid Droplets

Lewis and Pratt[1] observed that pendent drops containing solute which diffuses into the surrounding continuous phase sometimes showed ripples and pulsations at the interface; this was associated with increased rates of mass transfer. We have observed

similar behaviour with pendent drops of nitrobenzene, chlorobenzene, carbon tetrachloride and chloroform containing, as solutes, acetone, ethyl alcohol, methyl alcohol and *iso*propyl alcohol. The concentration of solute varied between 2 and 30 per cent.

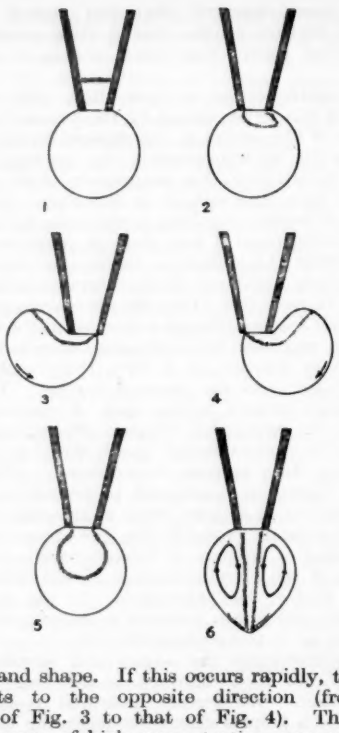
Drops were formed at the capillary end of a 25-ml. pipette. The rate of drop formation was controlled by regulating the flow of air into the pipette. Distilled water was used as the continuous phase, and the drops were formed at approximately 1 in. below the surface of the water. With the aid of suitable illumination and a visual reference system comprising a fine wire gauze behind the glass column containing the water, changes of refractive index, and thus the concentration gradients, both within and around the drops could be observed. Fine aluminium powder was suspended in the drop fluid so that any motion in the drops and also in the capillary could be seen.

There were marked differences in the pulsating behaviour and the type of motion within the drops, and these depended on: (*a*) rate of flow of the fluid into the drops (rate of drop formation); (*b*) concentration of solute; (*c*) nature of the liquids.

Very slow rates of drop formation (1–2 drops per min.). In the early stages of drop growth, the fluid near or at the water–drop interface revolved rapidly around the vertical axis of the capillary. After the drop had grown to approximately one-quarter of its maximum size, intermittent pulsations and rotation about a horizontal axis occurred, during which most of the solute diffused out of the drop. Between the pulsations the drop became motionless and there was no visible diffusion. Fig. 1 shows the drop when no pulsation or rotation is taking place. Fig. 2 shows the condition immediately before the start of pulsation. The shaded part in these diagrams represents a zone of sharp concentration gradient (often a cloudy layer) between the original liquid containing high concentration of solute and the drop fluid which has been depleted of most of its solute. The pulsation of the droplet and the rotation within the drop occurred only when this layer was within the drop.

Slow rates of drop formation (2–10 drops per min.). At slightly faster rates of formation, the period spent in the quiescent state diminished and the zone of concentration gradient was within the drop but near the end of the capillary (Fig. 2). It had a hemispherical or irregular shape and moved at random from side to side. Whenever the zone approached the drop–water interface a marked distortion of the shape of the drop rapidly developed (Figs. 3 and 4). Simultaneously rapid rotation around a horizontal axis (in clockwise or anti-clockwise direction) commenced within the drop, followed by a marked increase in the rate of mass transfer, mainly at the distorted part of the drop surface.

The direction of rotation was found to depend on the position of the zone of concentration gradient in relation to the drop–water interface. Fig. 3 shows a drop in which the zone has moved to the left-hand side and the direction of rotation is now anti-clockwise; Fig. 4 shows the rotation taking place in clockwise manner with the zone of concentration gradient on the right-hand side. With the depletion of solute at the small zone of high concentration (area above the line of shading), the interfacial tension around the whole of the surface becomes more uniform and the drop tends to resume its normal



position and shape. If this occurs rapidly, the drop overshoots to the opposite direction (from the position of Fig. 3 to that of Fig. 4). The hemispherical zone of high concentration now moves to the opposite side and the process is repeated, and results in a regular and continuous pulsation.

Medium rates of drop formation (10–30 drops per min.). The zone is now forced farther into the droplet and acquires an approximately spherical shape (Fig. 5). Diffusion takes place uniformly all around the drop surface. The surface zone of the drop is in continuous, irregular motion; but the shape of the droplet remains unaltered.

High rates of drop formation (30–45 drops per min.). The zone of concentration gradient takes the shape of a thin jet inside the drop (Fig. 6). There is a notable decrease in the radius of curvature of the surface at the lowest point in the drop and circulation occurs in the form of a vortex ring inside the drop. Diffusion mainly occurs near the pointed end where the solute concentration is highest.

At low concentrations of solute (1–5 per cent) the distortion of the drop shape, the pulsation and the motion within the drops were always much less than for higher concentrations.

Pulsation and circulation behaviour varied with the nature of both the solute and the solvent. For example, drops of 10 per cent ethyl alcohol and 90 per cent chlorobenzene showed a much more vigorous pulsation than drops of chlorobenzene with 10 per cent acetone as solute. Chlorobenzene solutions exhibited the phenomena more intensely than similar solutions of nitrobenzene. Chloroform and carbon tetrachloride systems showed much less pulsation and rotation.

The presence of small amounts of a surface-active compound in the aqueous phase (for example, 0·01 gm. sodium dodecyl sulphate in 1 lit. of distilled water) suppressed these phenomena. There was also

no visible diffusion of solute into the continuous phase for drops containing up to 10 per cent solute.

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Age of Uraninites from Crystallographic Data

In a recent communication, Wasserstein[1] has suggested a new method of age determinations on uraninites by means of X-ray techniques. This thesis is that radioactive decay results in the replacement of the tetravalent uranium ion by the smaller lead ion, the calculated shrinkage in cube edge due to this process being approximately 0·004 A. per hundred million years. Wasserstein classifies uraninites into three groups: γ(U_4O_7 type), α(UO_2 type) and β(U_3O_7 type), and suggests that thorianites, which resemble γ-uraninites in their properties, may have Th_4O_7 as their prototype.

We are of the opinion that this picture has been over-simplified and is not consistent with the known chemistry of the uranium oxides. In addition to the radioactive decay which tends to shrink the cube edge below that of pure uranium oxide, and the presence of thoria which serves to expand the lattice parameters, several other factors should be taken into consideration. Specifically these are: oxidation due to weathering, and radiation damage. As Wasserstein points out, oxidation of UO_2 to β-UO_3 results in a decrease in cube edge from 5·470 A. to 5·440 A. Every uraninite specimen for which an analysis has been reported has been shown to be oxidized to some extent; some are altered sufficiently so that ignition in vacuum or an inert atmosphere converts them partially or even completely to U_3O_8, and this oxidation should be reflected in the lattice parameter. In this regard, Wasserstein's classification of γ-uraninites as U_4O_7 types is questionable. The existence of U_4O_7 itself is based only on X-ray evidence[2] (an increase in cube edge above that of UO_2), and has as yet not been substantiated by chemical analyses. Assuming that U_4O_7 actually has been prepared, which is doubtful, the method of preparation in each case has involved extreme reducing conditions (that is, ignitions of mixtures of uranium oxide with uranium metal) which are not likely to be encountered in Nature. Extrapolation of this line of reasoning to suggest the existence of Th_4O_7 is, we believe, on even more doubtful ground since no experimental evidence exists for such a compound. Rather this phenomenon (contraction of the cube edge on ignition) in thorianite should suggest seeking an alternative explanation. It has been shown that radiation damage in a number of substances, including zircon, diamond, silicon carbide and quartz, results in an increase in lattice dimensions[3]. It would seem more reasonable to us to ascribe the γ-type ores to radiation damage than to reduction of uranium and thorium below the tetravalent state.

To the list of factors influencing lattice dimensions in uraninites should also be added the presence of rare-earth and alkaline-earth oxides, since these have been shown to form ternary fluorite-type oxides with uranium over a considerable oxygen to metal ion ratio range[4].

We feel that all these factors will play a significant part in determining uraninite lattice dimensions, thus making an age-calculation based on Wasserstein's proposal of doubtful value.

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The criticism offered by Drs. Hoekstra and Katz is relevant in stressing certain chemical difficulties which may defy solution by conventional analyses—mineral chemists know such problems too well, for example, the role of iron in many minerals. They rely on chemical analyses of uraninites for their views; but I am suspicious of such analyses as they still report lead as PbO, when that of radiogenic origin should be PbO_2; that due to, say, galena, would be correctly given as PbO. Such duality exists in the position of oxygen, too, as it takes a double role crystallographically in many uraninites—such data cannot adequately be determined chemically.

There must be grave doubts that the proportion of different uranium oxides, such as UO_2 and U_3O_8, are in fact present as such in uraninites. Controversy is still rife among chemists in this very field of uranium oxides. How then can Drs. Hoekstra and Katz state that my thesis ". . . is not consistent with the known chemistry of the uranium oxides"? The operative word is, I suggest, "known". I agree that, in the interests of clarity, I have simplified my concepts, but I trust I have not done this to a fault.

The essential points of the criticism, which carried no surprises, can be answered as follows:

(1) *Existence of U_4O_7 and Th_4O_7.* Actually these compounds are not essential for my thesis. At this stage it may be advisable to write γ-uraninite as UO_{2+x}. As experimental evidence indicates that oxidation is necessary to obtain the cube-edge of the corresponding α-type from the γ-type, an analogue of a lower oxide than UO_2 exists: Zachariasen's U_4O_7 is the closest laboratory counterpart. That the laboratory method of its preparation does not duplicate the conditions under which γ-type is formed in Nature is no criterion for the belief in the existence of the mineral or not.

All γ-uraninites are characterized by the presence of the large thorium ion; pitchblendes carry virtually none of it, but may contain such small ions as those of zirconium and titanium (for example, in Colorado). These replacements of uranium are in accordance with the principle that lower valence of an element is indicative of larger ionic size, and conversely. The different 'valencies' envisaged in my classification must have influenced the nature of the replacements at the time of the formation of the minerals. Such observations stress the individuality of the γ-type.

The fact that Th_4S_7 is known suggests that Th_4O_7 is possible; my statement that "U_4O_7 may be a separate compound analogous to Th_4S_7" was a

quotation in the text-book of which one of my critics is a co-author.

(2) *Weathering and oxidation.* Obviously highly weathered samples do not lend themselves to age determinations—they may not qualify even as uraninites. Sample selection largely obviates such difficulties, especially when the minuteness of the material required for X-ray determinations is considered. Heat treatment, particularly as used for γ-types, further helps to limit, and also recognize, this factor. The effect of oxidation should not be over-emphasized, as in some samples the effect on the parameter proved less than the error in determination.

The material used for the tabulated results is above reproach.

(3) *Radiation damage.* This is a negligible factor here, except perhaps in comparatively young pitchblendes. To try to explain γ-uraninites by increase in lattice parameter brought about by radiation immediately poses the question of the other two types: Why are these not similarly affected? The suggestion cannot explain the chemical differences observed.

(4) *Presence of rare-earths and alkaline-earths.* Sample selection by the avoidance of nivenites and cleveites controlled the effect of the omnipresence of the rare-earths. These elements generally depress the parameter but, in the samples used, such reduction is negligible. The role, if any, of the alkaline-earths is inconsequential here.

I thank Drs. Hoekstra and Katz for their criticism, but it has offered no explanation of the regularity observed in my table of results; they infer that results may show haphazard values. If cube-edges of uraninites are considered in the light of my thesis, a fine order is found to exist where chaos now reigns.

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Age of the Mineralization of the Witwatersrand

Louw[1] has recently reported new isotopic assays of radiogenic lead from the uraninites of the Witwatersrand, and has utilized these data in arguments supporting a placer origin for the Rand mineralization. The same information has been published in fuller extent elsewhere[2], and a third paper by the same author, already circulated in preprint form, is in the press[3].

These arguments based upon mass-spectrographic analyses form the sole response of South African scientists to the criticisms of the placer theory which I have published in recent years[4]. A refutation of Louw's conclusions awaits printing elsewhere[5]; and since repetitive publication is to be deprecated, it will suffice to note here that much of the latest South African work is vitiated by the lack of mineragraphic control of the uraninite samples studied, which were greatly contaminated by galena of unknown isotopic composition. Restricting attention to measurements on the less impure samples carrying upwards of about 50 per cent uranium, there are now nine $^{207}Pb : ^{206}Pb$ ages available for Witwatersrand uraninite, determined by four different laboratories. These ages uniformly fall within the average of 2,055 ± 150 million years, a result in good agreement with the dating of 2,080 ± 40 million years arrived at by Holmes[6] for the Limpopo granitization nearby. Age determinations therefore lend support to the already weighty arguments favouring an epigenetic origin for the Rand ores by pointing, for the first time, to a cycle of granitization with which the mineralization may be connected.

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[6] Holmes, A., *Col. Geol. Min. Res.*, **5**, 3 (1955).

A New Joule Manuscript

In 1851, William Hopkins, of Cambridge, obtained a grant of £250 from the Government "for investigations on the effect of pressure on the temperature of fusion of certain substances". It was stipulated that expenditure of the money should be under the control of a committee which included Joule.

During the next few years Hopkins, Joule and William Fairbairn worked in close co-operation on these problems, and Hopkins reported some of their findings (which were not recorded) to the Hull meeting of the British Association in September 1853. This report would certainly include results given in a letter, written by Joule, and recently found in a volume of Watts's translation of "Gmelin's Hand-Book of Chemistry" (which once belonged to Joule and is now in the Manchester College of Technology Library). Joule gives details of a series of experiments he did on the physical properties of beeswax "which may perhaps serve to throw some light on the alteration of the point of liquefaction by pressure".

It is addressed to William Hopkins from Acton Square, Salford, and is dated August 20, 1853. It would appear to be a draft, because in a letter dated August 24 to Fairbairn[1] giving him only a brief outline of the results, Joule says: "I transmitted to Mr. Hopkins yesterday . . .", that is, three days later than the date on the letter recently found.

There are twelve small pages, and the first eight give details of nine experiments carried out to determine the specific heat of wax at differing temperatures and the heat absorbed in changing the state of one grain of wax from perfect solidity to perfect fluidity. Joule remarks: "having no exact point at which perfect solidity is followed by perfect fluidity, our 'stationary point' (Hopkins's term) was entirely delusive". The remaining four pages are devoted to the expansion by heat of beeswax, in which Joule uses a formula of William Thomson. He finishes by saying: "the experiments which I have related are worth repeating and with greater accuracy. This, however, would require apparatus for the purpose and more time than I shall have at my disposal for some weeks to come. I hope, however, that the above results, such as they are, will not be without their use in formulating your views".

The letter may be seen in the College of Technology Library, Manchester.

L. L. Ardern

College of Technology,
Manchester. Feb. 11.

[1] Pole, William, "Life of Sir William Fairbairn", 296 (1877).

FORTHCOMING EVENTS

Monday, April 4

BRITISH OCCUPATIONAL HYGIENE SOCIETY (at the London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1), at 11 a.m.—Discussion on "The Assessment of Health and Disease in Industry".

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 5 p.m.—Mr. R. D. Hayes: "Cambridge Expedition to Ancora (North Portugal)".

NORTH EAST COAST INSTITUTION OF ENGINEERS AND SHIPBUILDERS (in the Lecture Theatre of the Mining Institute, Newcastle-upon-Tyne), at 6.15 p.m.—Mr. S. G. Lankester and Mr. W. D. Wallace: "Some Investigations into Singing Propellers".

Monday, April 4—Tuesday, April 5

SOCIETY OF CHEMICAL INDUSTRY, LONDON SECTION (in the William Beveridge Hall, Senate House, University of London, W.C.1), at 9.30 a.m. daily—Symposium on "The Prevention of Atmospheric and Water Pollution in the Chemical Industry".

Monday, April 4—Wednesday, April 6

FARADAY SOCIETY (in the Department of Zoology, Cambridge University)—General discussion on "Microwave and Radio-Frequency Spectroscopy".

INSTITUTION OF NAVAL ARCHITECTS (in the Weir Lecture Hall, 10 Upper Belgrave Street, London, S.W.1)—Spring Meeting.

Wednesday, April 6

At 10.15 a.m.—Annual General Meeting.

Tuesday, April 5

ZOOLOGICAL SOCIETY OF LONDON (at the Zoological Gardens, Regent's Park, London, N.W.1), at 5 p.m.—Scientific Papers.

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENTS AND RADIO SECTIONS (at Savoy Place, London, W.C.2), at 5.30 p.m.—Dr. D. M. MacKay: "High Speed Electronic-Analogue Computing Techniques".

Wednesday, April 6

ROYAL ASTRONOMICAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Prof. Dirk Brouwer: "Motions of the Outer Planets" (George Darwin Lecture).

GEOLOGICAL SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Scientific Papers and Films.

INSTITUTION OF POST OFFICE ELECTRICAL ENGINEERS (at the Institution of Electrical Engineers, Savoy Place, Victoria Embankment, London, W.C.2), at 5 p.m.—Mr. F. Moxon: "Regional Problems in the Provision and Maintenance of V.H.F., U.H.F., and S.H.F. Radio Links".

SOCIETY FOR ANALYTICAL CHEMISTRY, PHYSICAL METHODS GROUP (at the Chemical Society, Burlington House, Piccadilly, London, W.1), at 7 p.m.—Scientific Papers.

SOCIETY FOR VISITING SCIENTISTS (at 5 Old Burlington Street, London, W.1), at 7.30 p.m.—Discussion on "Allergy: Current Conceptions". Chairman: Sir Henry H. Dale, O.M., F.R.S.: Speakers: Dr. Bernard N. Halpern, Prof. J. R. Marrack and Dr. J. Pepys.

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

ASSISTANT, Grade B (with a degree or equivalent qualification) IN INORGANIC CHEMISTRY—The Principal, Slough College for Further Education, William Street, Slough (April 9).

CHEMIST (with a degree in chemistry or equivalent qualifications and a sound knowledge of modern instrument techniques, and with experience in investigational and research work, and ability to lead a small research group), at the Central Laboratory, Shade House, Pendlebury, Manchester—The Establishment Office, National Coal Board, 40 Portland Street, Manchester 1 (April 9).

LECTURER (with an honours degree and also appropriate qualifications in agriculture, and with experience of research and teaching in field experimentation) IN FIELD EXPERIMENTATION—The Secretary, School of Agriculture, University of Cambridge, Downing Street, Cambridge (April 13).

ASSISTANT, Grade B (with a degree or equivalent qualification in mining or geology, and preferably with practical experience in the coal mining industry) IN THE DEPARTMENT OF MINING, to teach geology to general certificate of education advanced level and to higher national certificate standard in the mining and mine surveying courses—The Registrar, Nottingham and District Technical College, Shakespeare Street, Nottingham (April 14).

LECTURER, Grade I, or LECTURER, Grade II, IN AGRICULTURAL ECONOMICS AND FARM MANAGEMENT, and an ASSISTANT LECTURER IN ANIMAL HUSBANDRY, at the University College, Ibadan—The Secretary, Inter-University Council for Higher Education Overseas, 1 Gordon Square, London, W.C.1 (April 15).

ASSISTANTS IN MATHEMATICS—Secretary of University Court, The University, Glasgow (April 16).

CHEMIST, Senior Scientific Officer grade (with an honours degree or equivalent, and postgraduate research experience in physical chemistry, preferably on the properties of surfaces or of high polymers), at a Ministry of Supply Research Establishment near Salisbury, Wilts, to take charge of a small team undertaking research on permanently biocidal coatings—The Ministry of Labour and National Service, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting F.173/5A (April 16).

READER or SENIOR LECTURER IN CHEMISTRY, and LECTURERS or ASSISTANT LECTURERS (2) IN CHEMISTRY, at the University College of Khartoum, Sudan—The Secretary, Inter-University Council, 1 Gordon Square, London, W.C.1 (April 21).

CHAIR OF AGRICULTURE at the University College of Khartoum, Sudan—The Secretary, Inter-University Council, 1 Gordon Square, London, W.C.1 (April 22).

VETERINARY BACTERIOLOGIST, Senior Research Officer or Research Officer grade (with a university degree in veterinary science, with postgraduate research experience in bacteriology or immunology, or equivalent qualifications) IN THE ANIMAL HEALTH RESEARCH LABORATORY, Commonwealth Scientific and Industrial Research Organization, Parkville, Victoria, Australia, to undertake research work on aspects of bovine contagious pleuropneumonia—Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2, quoting 201/74 (April 23).

ASSISTANT LECTURER (with an honours degree in geology and an interest in palæontology and Palæozoic stratigraphy) IN GEOLOGY—The Secretary, University College, Gower Street, London, W.C.1 (April 25).

LECTURER (with special experience of X-ray crystallography) IN CHEMICAL PHYSICS OF SOLIDS in the Department of Chemical Engineering—Head of the Department of Chemical Engineering, Imperial College, London, S.W.7 (April 25).

CHAIR OF PHYSICAL METALLURGY—The Registrar, University College, Singleton Park, Swansea (April 30).

CHAIR OF VETERINARY PATHOLOGY—The Registrar, The University, Liverpool (April 30).

JUNIOR FELLOW (preferably with experience in fluid mechanics) IN APPLIED MATHEMATICS—The Registrar and Secretary, The University, Bristol (April 30).

LECTURER IN PHYSICS, at Rhodes University, Grahamstown, South Africa—The Secretary, Association of Universities of the British Commonwealth, 5 Gordon Square, London, W.C.1 (South Africa, April 30).

LECTURER IN PSYCHOLOGY; a LECTURER IN METAL PHYSICS, and a LECTURER (with special interests in fluid mechanics) IN ENGINEERING—The Registrar, University College, Singleton Park, Swansea (April 30).

LEICESTER LOVELL RESEARCH STUDENT, to study the mechanism and kinetics of reactions of epoxides—Professor of Chemistry, The University, Southampton (April 30).

ASSISTANT CURATOR (with an honours degree in some branch of natural science including zoology, and preferably with museum experience) OF INVERTEBRATES in the Museum of Zoology—Dr. A. S. Watt, Botany Department, University of Cambridge, Downing Street, Cambridge (May 1).

ASSISTANT LECTURER IN PHYSICS—The Registrar, University College of North Staffordshire, Keele, Staffs (May 1).

ENGLISH ELECTRIC RESEARCH FELLOW IN AERONAUTICS—The Warden, College of Aeronautics, Cranfield, Bletchley, Bucks (May 1).

LECTURER IN ASIAN ANTHROPOLOGY—The Secretary, School of Oriental and African Studies, University of London, W.C.1 (May 1).

LECTURER (medical qualification not essential) IN THE DEPARTMENT OF BACTERIOLOGY—The Registrar, The University, Liverpool (May 1).

CHAIR OF PARASITOLOGY tenable at the Imperial College of Science and Technology, London, S.W.7—The Academic Registrar, University of London, Senate House, London, W.C.1 (May 3).

READER IN GEOLOGY at King's College, Strand, London, W.C.2—The Academic Registrar, University of London, Senate House, London, W.C.1 (May 5).

RESEARCH OFFICER (Rheologist) (with a university honours degree in science, with physics and/or chemistry as a major subject or equivalent qualifications) IN THE DIVISION OF BUILDING RESEARCH, Commonwealth Scientific and Industrial Research Organization, Highett, Victoria, Australia, for investigations into the rheological characteristics of building materials—Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2, quoting 390/204 (May 21).

ELLISON RESEARCH FELLOWS (graduates of British universities) IN CHEMISTRY or PHYSICS; and a RESEARCH SCHOLAR for research work connected with the chemistry of amino-acids, peptides and proteins—The Registrar, The University, Sheffield (June 1).

ROYAL DUTCH SHELL STUDENT IN GEOPHYSICS—The Registrar, Imperial College of Science and Technology, London, S.W.7 (June 1).

ASSISTANT LECTURER IN INORGANIC CHEMISTRY—Prof. Barrer, Chemistry Department, Imperial College, London, S.W.7.

BIOCHEMIST, Basic grade (with a science degree or A.R.I.C. diploma)—The Group Secretary, Walsall General Hospital, Walsall, Staffs.

LABORATORY TECHNICIAN (preferably with a knowledge of photography), to assist in the care of animals and in biological experiments, and to prepare specimens for microscopical examination—The Director, B.E.C.C. Research Unit in Radiobiology, Mount Vernon Hospital, Northwood, Middlesex.

LABORATORY TECHNICIAN (with experience of food and toxicological analysis) IN THE DEPARTMENT OF VETERINARY HYGIENE AND PREVENTIVE MEDICINE, University of Edinburgh—The Secretary, The University, Old College, South Bridge, Edinburgh.

LECTURER (with a degree in biochemistry and/or chemistry, including organic chemistry taken to an advanced stage, and preferably with experience in the analysis of foods, including dairy products) IN AGRICULTURAL BIOCHEMISTRY, at Massey Agricultural College (University of New Zealand), Palmerston North—The Secretary, Association of Universities of the British Commonwealth, 5 Gordon Square, London, W.C.1.

LIVESTOCK OFFICER (with a university degree either in dairy husbandry or in agriculture with specialization in animal husbandry, and some experience in stock management) IN THE VETERINARY DEPARTMENT, Nyasaland, for duties connected with the development of the local animal industry, mainly in African areas—The Director of Recruitment, Colonial Office, Sanctuary Buildings, Great Smith Street, London, S.W.1, quoting BCD 67/4/03.

SCIENTIFIC OFFICER (with at least a first- or second-class honours degree in mathematics or physics and a thorough practical and theoretical knowledge of geometrical optics) to carry out research in instrument requirement assessment and also to apply this research to the design of a wide variety of optical instruments including photographic lenses—The Senior Recruitment Officer, Atomic Weapons Research Establishment, Aldermaston, Berks, quoting 550/WGE/2.

SENIOR SCIENTIFIC OFFICER or SCIENTIFIC OFFICER (honours graduate with research ability, and preferably with experience of small-scale metal fabrication), at the Atomic Energy Research Establishment, Harwell, to work on the application of novel and unconventional techniques to fundamental research on the fabrication of an unusual metal—The Establishment Officer, Atomic Energy Research Establishment, Harwell, Didcot, Berks, quoting 2/103/259.

TRAINED TECHNICIAN IN THE BOTANY DEPARTMENT—The Registrar, University College of Wales, Aberystwyth.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

"The Earth is the Lord's." By the Rev. C. E. Raven. (An address to the 1954 Conference of the Institute of Rural Life at Home and Overseas.) Pp. 12. (London: Institute of Rural Life at Home and Overseas, 1954.) 6*d*. [71

British Hat and Allied Feltmakers Research Association. Seventh Annual Report of the Director of Research for the year ending August 1954. Pp. 19 (2 plates). (Manchester: British Hat and Allied Feltmakers Research Association, 1954.) [71

Department of Scientific and Industrial Research. Forest Products Research. Bulletin No. 33: The Strength Properties of Plywood. Part 2: Effect of the Geometry of Construction. By W. T. Curry. Pp. iv+28+4 plates. (London: H.M. Stationery Office, 1954.) 2*s*. net. [71

Bulletin of the British Museum (Natural History). Zoology. Vol. 2, No. 9: A Collection of Mesostigmatid Mites from Alaska. By G. Owen Evans. Pp. 285–307. 7*s*. Entomology. Vol. 3, No. 13: Revisional Notes on the Genus *Epitola* Westwood (Lepidoptera: Lycaenidae). By Patrick Roche. Pp. 489–502+plates 19–22. 8*s*. Vol. 3, No. 14: African Species of the Genus *Pardomima* Warren (Lepidoptera: Pyralisae: Pyraustinae). By Edward L. Martin. Pp. 503–521+plate 23. 7*s*. (London: British Museum (Natural History), 1954 and 1955.) [71

British Museum (Natural History). British Antarctic ("Terra Nova") Expedition, 1910. Natural History Report. Geology. Vol. 2, No. 1: The Volcanic Rocks of the Ross Archipelago. By W. Campbell Smith. Pp. 107+6 plates and 2 maps. (London: British Museum (Natural History), 1954.) 60*s*. [71

National Parks and Access to the Countryside Act, 1949. Fifth Report of the National Parks Commission for the year ending 30th September 1954. Pp. iv+56+8 plates. (London: H.M. Stationery Office, 1954.) 3*s*. 6*d*. net. [101

Ministry of Fuel and Power. Reports of H.M. Inspectors of Mines under the Coal Mines Act, 1911, for the year 1953. North Western Division. By G. Hoyle. Pp. ii+26+5 plates. 2*s*. net. East Midland Division. By W. B. Brown. Pp. ii+20. 1*s*. net. (London: H.M. Stationery Office, 1954.) [101

Ministry of Education. Early Leaving: a Report of the Central Advisory Council for Education (England). Pp. vii+99. (London: H.M. Stationery Office, 1954.) 3*s*. 6*d*. net. [111

Science and Religion: a Changing Relationship. By Prof. C. A. Coulson. (Rede Lecture for 1954.) Pp. 36. (Cambridge: At the University Press, 1955.) 2*s*. 6*d*. net. [111

British Social Biology Council. Alpha and Omega: a Study of some Religious and Biological Teaching in Schools on the Origin of Life and of Man. By Dr. L. M. J. Kramer. (Educational Paper No. 7.) Pp. 22. (London: British Social Biology Council.) 1*s*. 9*d*. [211

Privy Council. Medical Research Council Memorandum No. 29: Indices of Heat Stress—a Statistical Comparison of Effective Temperature and an Index based on Sweat Loss. By F. E. Smith. (A Report based on experiments carried out at the National Hospital for Nervous Diseases, Queen Square, London, by B. McArdle, W. Dunham, H. E. Holling, W. S. S. Ladell, J. W. Scott, M. L. Thomson and J. S. Weiner.) Pp. 52. (London: H.M. Stationery Office, 1955.) 2*s*. net. [211

Other Countries

Imperial College of Tropical Agriculture. A Report on Cacao Research, 1953. Pp. 87 (11 plates). (St. Augustine, Trinidad and London: Imperial College of Tropical Agriculture, 1954.) [71

United States Naval Observatory. Circular No. 53: Annular Eclipses 1958, 1959. By Simone Daro Gossner. Pp. 4. Circular No. 54: Positions, Areas, and Counts of Sunspots, July–August, 1954. By Winifred Sawtell Cameron. Pp. 4. (Washington, D.C.: U.S. Naval Observatory, 1954.) [71

Bulletin of the Museum of Comparative Zoology at Harvard College. Vol. 112, No. 3: Status of Invertebrate Paleontology, 1953. Edited by Bernhard Kummel. Pp. 91–318. Vol. 112, No. 4: Revision of the Chrysomelid Subfamily Aulacoscelinae. By F. Monrós. Pp. 319–360. (Cambridge, Mass.: Museum of Comparative Zoology at Harvard College, 1954.) [71

Institut pour la Recherche Scientifique en Afrique Centrale. Pp. 14+13 plates. (Bruxelles: l'Institut pour la Recherche Scientifique en Afrique Centrale, 1954.) [71

Colony of Mauritius. Annual Report of the Observatory Department for the year 1953. Pp. 1+16. (Port Louis: Government Printer, 1954.) [71

Royal Alfred Observatory, Mauritius. Results of Magnetical and Meteorological Observations. July, 1950. Pp. 14. August, 1950. Pp. 14. September, 1950. Pp. 14. October, 1950. Pp. 14. November, 1950. Pp. 14. December, 1950. Pp. 16. (Port Louis: Government Printer, 1954.) [71

Carnegie Institution of Washington. Report of the President for the year ending June 30, 1954. Pp. 15. (Washington, D.C.: Carnegie Institution of Washington, 1954.) [71

Central Laboratories for Scientific and Industrial Research, Hyderabad. Annual Report, 1953. Pp. x+64. (Hyderabad-Deccan: Central Laboratories for Scientific and Industrial Research, 1954.) [71

Metropolitan Life Insurance Company. Statistical Bulletin, Vol. 35, No. 11: Improved Outlook for Surgical Patients. Pp. 12. (New York: Metropolitan Life Insurance Company, 1954.) [101

The Geophysical Observatory: a Study in Technical Assistance. Pp. 35+4 plates. (Karachi: Ministry of Education, 1954.) [111

Bibliography of Scientific Publications of South Asia (India, Burma, Ceylon). No. 10: July–December, 1953. Pp. iii+158. (New Delhi: Unesco, South Asia Science Co-operation Office, 1954.) [211

Research Bulletin of the Panjab University. Nos. 49–50 (Zoology): On Three New Species of the Genus *Cephalogonimus* Poirier, 1886, from the Intestine of *Lissemys Punctata Punctata*. On Five New Trematodes of the Genus *Astiotrema* Looss, 1900, from the Intestine of *Lissemys Punctata Punctata*, and discussion on the Synonymity of Two Already Known Forms. By Dr. N. K. Gupta. Pp. 71–100. 3 rupees. No. 51 (Zoology): Taxonomic Values of Chromosomes and Cytoplasmic Inclusions in a Digenetic Trematode—*Phyllodistomum Spatula*. By Om Parkash Dhingra. Pp. 101–109. 1 rupee, 7 annas. No. 52 (Chemistry): The Phenomenon of Continuous Freezing of Capillary-held Water at Decreasing Temperatures. By Balwant Rai Puri, Lakh Raj Sharma and M. L. Lakhanpal. Pp. 111–116. 15 annas. No. 53 (Zoology): On *Mehraorchis Tigrinarum*, a New Species from the Stomach of *Rana Tigrina*. By Dr. N. K. Gupta. Pp. 117–120. 12 annas. No. 54 (Zoology): On a New Species of the Genus *Ommatobrepha* Nicoll, 1914, from the Intestine of *Natrix Piscator* in Ludhiana. By Dr. N. K. Gupta. Pp. 121–123. 10 annas. No. 55 (Zoology): On a New Species of the Genus *Ganeo* Klein, 1905, from the Intestine of *Rana Cyanophlyctis*. By Dr. N. K. Gupta. Pp. 125–129. 12 annas. No. 56 (Zoology): On Two New Species of Trematode Parasites from Birds in Hoshiarpur. By Dr. N. K. Gupta and B. K. Dhillon. Pp. 131–137. 1 rupee. No. 57 (Zoology): On *Encyclometra Vitellata*, a New Species from Water-Snail, *Natrix Piscator*. By Dr. N. K. Gupta. Pp. 139–141. 10 annas. No. 58 (Zoology): On *Pleurogenes* (*Teloganella*) *Savanesis*, N. SP., Parasitic in the Intestine of *Rana Cyanophlyctis*, with a discussion on the Systematic Position of the Genus *Pleurogenes* Looss, 1896. By Dr. N. K. Gupta. Pp. 143–148. 14 annas. No. 59–60 (Zoology): Microphotographs Demonstrating the Vacuome, Golgi Bodies, Mitochondria and Nucleolar Extrusions in the Fresh Eggs of Frog as studied under the Phase Contrast Microscope. By Vishwa Nath and Kumar Malhotra. An Examination of the Yolk-Nucleus of the Spider *Plexippus Paykulli* under the Phase Contrast Microscope. By Vishwa Nath and Rajindar M. Dhawan. Pp. 149–157. 1 rupee, 7 annas. No. 61 (Zoology): Spermatogenesis of a Digenetic Trematode *Cyclocoelum Biversiculatum*. By Om Parkash Dhingra. Pp. 159–168. 1 rupee, 12 annas. No. 62 (Zoology): Fish Spermatogenesis with particular reference to the fate of the Cytoplasmic Inclusions. 3: Spermatogenesis of Actinopterygii (Cyprinodontidae). By Hem Sagar Vasisht. Pp. 169–175. 1 rupee, 2 annas. (Hoshiarpur: Panjab University, 1954.) [211

Annual Report of the Kodaikanal Observatory for the year 1953. Pp. 10. (Delhi: Manager of Publications, 1954.) 9 annas; 10*d*. [21

Faculty of Science: Osaka University. Annual Report of Scientific Works. Vol. 2. Pp. 125 (2 plates). (Osaka: Faculty of Science, Osaka University, 1954.) [211

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World Health Organization. Technical Report Series. No. 90: Bilharzia Snail Vector Identification and Classification (Equatorial and South African). Report of a Study Group. Pp. 22. 1 Swiss franc; 1*s*. 9*d*. net; 0.25 dollars. No. 91: Expert Committee on Nursing. Third Report. Pp. 28. 1 Swiss franc; 1*s*. 9*d*. net; 0.25 dollars. (Geneva: World Health Organization; London: H.M. Stationery Office, 1954.) [211

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